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Reduction of *cis*-Bicyclo[4.3.0]non-3-ene and Its 8-Substituted Heterocyclic Analogues

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Abstract: The preparation and competitive catalytic hydrogenation of members of the 8-heterobicyclo[4.3.0]non-3-ene series are discussed. The heteroatom's specific coordination with the catalyst is rationalized as the origin of the observed heteroatom effects.

During the past several years, we have been interested in the ways a heteroatom influences the structure and reactivity of nonaromatic heterocyclic molecules.[1] As part of this continuing study, we embarked on an analysis of the catalytic reduction of various members of the *cis*-8-heterobicyclo[4.3.0]non-3-ene series. Of particular interest in this series is the skeletal similarity, which enables us to examine how the heteroatom expresses its effects throughout the molecule. The preparations of these compounds are outlined in Scheme I.

The commercially available anhydride **1** was reduced with lithium aluminum hydride to **2**.[2] Treatment of **2** with *p*-toluenesulfonyl chloride in refluxing pyridine resulted in a high-yield conversion to *cis*-8-oxabicyclo[4.3.0]non-3-ene (**3**).[3] Tosylation of **2** at 0 °C yielded **5**. Refluxing an ethanolic solution of **5** with sodium sulfide[4] produced *cis*-8-thiabicyclo[4.3.0]non-3-ene (**4**). Cyanide displacement of the tosylate groups on **5** gave the dinitrile **6**,[5] which was immediately converted to **7**[5] by hydrolysis. Ruzicka cyclization of **7** produced **8**, which after Wolff-Kishner reduction gave *cis*-bicyclo[4.3.0]non-3-ene (**9**).[5] *cis*-8-Azabicyclo[4.3.0]non-3-ene (**11**) was prepared by the lithium aluminum hydride reduction of **10**.[1b]

Although we were aware of the possibility of ring-juncture epimerization by palladium catalysts, the short reaction times anticipated for our studies suggested that we examine this metal, particularly with the potential for catalyst-heteroatom studies. Because of the simplicity of preparation, the test compounds used were **3** and *trans*-8-oxabicyclo[4.3.0]non-3-ene (**16**).[15] The preparation of **16** is presented in Scheme II. Diethyl fulmarate and butadiene were allowed to undergo a Diels-Alder reaction to yield **14**. Reduction of the diester with lithium aluminum hydride gave the trans diol **15**, which was converted to **16** by the action of *p*-toluenesulfonyl chloride in hot pyridine.

Hydrogenation of **3** with 10% Pd–C at 20 psi hydrogen pressure in a Parr hydrogenation apparatus for 30 min resulted in a complex reaction mixture, as judged by examination of the GLC chromatogram. By comparing aliquots with authentic samples of the reduction products, **17** and **18**, through the reaction conditions, we were able to determine that simple product epimerization was not occurring.

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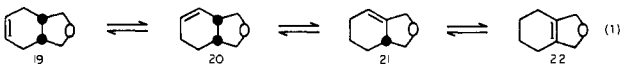
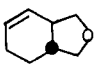
17 18

A combination of NMR and mass spectral examination of the product mixture indicated that for **3** alkene isomerization was taking place according to the scheme shown in eq 1.



19 20 21 22 (1)

Specifically, collection of the various isomers by preparative GLC followed by NMR integration of vinyl protons for each isomer gave strong evidence for the identities of **20** and **21**. The structure of **22** was confirmed by an unambiguous synthesis.[6] It is of interest that we could find no evidence for double-bond migration in **16**. Dreiding models suggest too much strain in **23** to make this a favorable process.



23

After examining several catalyst and support combinations, we selected 5% platinum on alumina for our experiments. This catalyst system resulted in a useful reduction without complications of isomerization.

In the competitive reductions of two alkenes, A and B, the following expressions can be written:[7]

$$\frac{-dC_A}{dt} = \frac{k_A K_A C_A}{(1 + K_A C_A + K_B C_B)} \quad (2)$$

$$\frac{-dC_B}{dt} = \frac{k_B K_B C_B}{(1 + K_A C_A + K_B C_B)} \quad (3)$$

where C = concentration, k = rate constant, and K = adsorption equilibrium constant. By combining (2) and (3), and defining

$$R_A \equiv \frac{-dC_A}{C_A\,dt} \; R_B \equiv \frac{-dC_B}{C_B\,dt} \quad (4)$$

we obtain

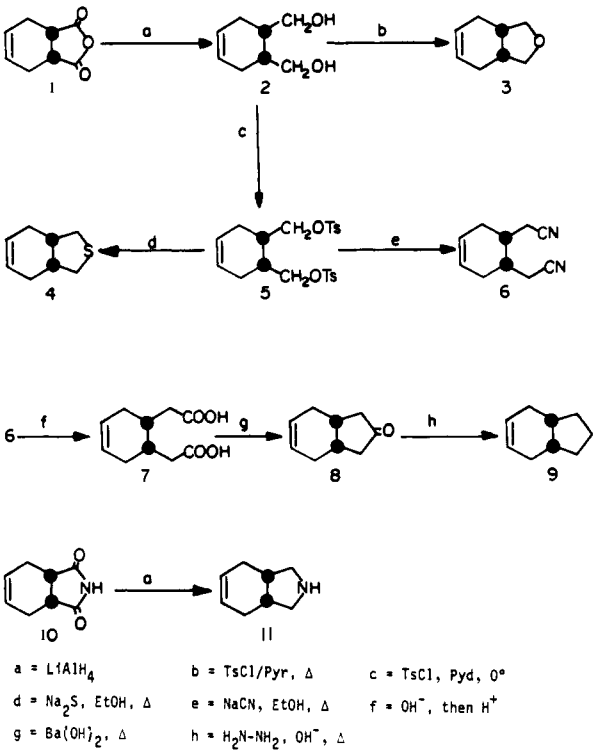
$$\frac{R_B}{R_A} = \frac{k_B K_B}{k_A K_A} = \frac{\log (C_{B_i}/C_B)}{\log (C_{A_i}/C_A)} \quad (5)$$

The competition ratio thus obtained is a composite of the reduction rate and the adsorption equilibrium between the substrate and the catalyst.[8] These equations are based on the assumption that the reaction rate is proportional to the surface concentration of adsorbed substrate.

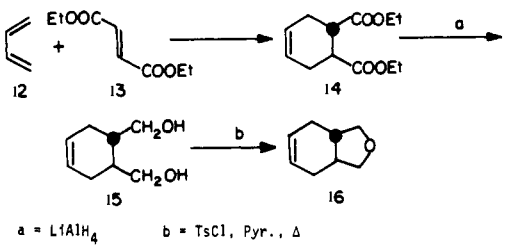
The ratio, R_B/R_A, should be constant over a reasonable period of time. For our work we were going to stop the reaction long before completion of reduction and utilize only the data obtained competitively from one reaction time. This competitive technique has had experimental verification from many investigators.[9] However, to be assured that the approach was reasonable, we examined the competition of **9** and cyclohexene for a period of 1 h, sampling the reaction for duplicate analysis every 15 min. The results of this experiment are summarized in Figure 1, where the experimental error is indicated by the size of the data points. By examining the slopes for the two reactions, we find that the slope for **9** is 4.4 times greater than that for cyclohexene. The correlation coefficient for the slope for **9** is 0.998, while that for cyclohexene is 0.994.

With linearity of the reaction established, the competitive experiments were initiated. Each of the alkenes **3**, **4**, **9**, and **11** (1 mmol) was mixed with an equal molar amount of freshly purified cyclohexene and 0.0025 g of catalyst in 1.0 mL of absolute ethanol in a test tube. A series of test tubes was placed in a Parr hydrogenation flask, and hydrogenation was performed at 20 °C for 30 min at 20 psi hydrogen pressure, except for reactions involving **11**. These proved to be so sluggish that the pressure was increased to 40 psi. Three independent runs of each competition were carried out, and the extent of hydrogenation was monitored by quantitative GLC. For each compound analyzed, an appropriate calibration curve had been prepared so that a detector response factor could be included in the analysis. The results from this study are summarized in Table I.

Scheme I. Preparations of 8-Substituted Members of *cis*-Bicyclo[4.3.0]non-3-ene Series



Scheme II. Preparation of *trans*-8-Oxabicyclo[4.3.0]non-3-ene



From these data, each of the members of the *cis*-bicyclo[4.3.0]non-3-ene (with the exception of **4**, and sulfides are well established as catalyst poisons[10]) appears more reactive than cyclohexene. However, we cannot discount the effects of the substrate-catalyst interaction. To place the steps in proper perspective, it is appropriate to examine a mechanistic interpretation of the reduction process (eq 6-10).

$$H_2 + ** \rightarrow 2H^* \quad (6)$$

$$A + ** \rightleftarrows {}^*A^* \text{ (adsorption)} \quad (7)$$

$${}^*A^* + H^* \rightleftarrows {}^*AH + ** \text{ (H transfer)} \quad (8)$$

$${}^*AH + H^* \rightarrow {}^*AH_2^* \text{ (H transfer)} \quad (9)$$

$${}^*AH_2^* \rightarrow AH_2 + ** \text{ (desorption)} \quad (10)$$

where A = alkene; AH_2 = reduction product; ** = catalytic sites. In this interpretation, the formation and desorption of AH_2 are irreversible, and catalytic sites are made available. Additionally, it has been established[10] that the order of platinum complexing is alkene > hydrogen ≫ alkane. It is noted

Table I. Relative Competition Ratios

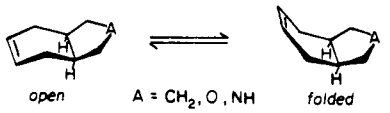
compd	3 (O)	4 (S)	9 (CH_2)	11 (NH)
R/R cyclohexene	6.59 ± 0.73	very slow[a]	4.92 ± 0.20	23.63 ± 1.59

[a] No measurable reduction of either 4 (S) or cyclohexene.

again in this analysis that the alkene-catalyst interaction will have a strong influence on the rate of the reduction process.

A rationalization for the observed reactivities makes use of the catalyst-substrate interactions. For **4**, the well-noted poisoning effects of divalent sulfur compounds can be seen in the absence of measurable reduction for either **4** or cyclohexene. In this study **11** is seen to reduce considerably faster than cyclohexene. However, the need for increased hydrogen pressure in order to make these reductions occur at a reasonable rate suggests not so much an increased reactivity of **11** as a decreased reactivity of cyclohexene. Amines have been identified as mild catalyst poisons, i.e., molecules which tend to preempt active sites to the exclusion of alkenes and/or hydrogen. Hence, it is not surprising that **11** competes effectively against cyclohexene. In fact, a favorable chelative geometry in **11** may allow its alkene and nitrogen functions, acting together, to compete even more effectively against cyclohexene than a saturated amine would. In addition, because of the known "poisoning" behavior of amines, even after reduction, the sites which had been complexing with the alkene may not be immediately made available for other molecules, hence the slow overall rate of reduction. Indeed, the nitrogen-platinum interaction results in the rest of the molecule sterically hindering approach of even the smaller molecule, cyclohexene, to the platinum surface (Figure 2).[11]

At this time, it is premature to ascribe a particular orientation of the molecule to the catalyst surface, since this series of experiments did not allow us to know the direction of hydrogen delivery to the alkene bond. We will be examining this question with a related series in the near future. We do note, however, that the conformational inhomogeneity associated with members of the *cis*-bicyclo[4.3.0]non-3-ene series[1] will be an additional problem warranting study (eq 11). How cat-



(11)

alytic surfaces will influence the preferred interaction conformation, or how either conformer rests on a catalyst surface, is not known.

The importance of molecular architecture in determining reactivity in these series is hinted at in the observation that in competitive hydrogenation **16** is 1.33 ± 0.03 times more reactive than cyclohexene. This is about one-fifth as reactive as the cis counterpart (**3**) and suggests the importance of the exact heteroatom-alkene bond juxtaposition. It is of interest to note, as a comparison, that oxymercuration of **3** occurs at about twice the rate as for **16**.[1c] A Dreiding model for the *open* conformation of **3** is remarkably similar to **16**, thus making it difficult to rationalize reactivity differences. Much remains to be done.[12]

A similar analysis is appropriate for **3**. The decrease in relative reactivity, compared to **11**, can be attributed to the oxygen-platinum interaction being less than the nitrogen-platinum interaction. As an additional consequence of this, the reduction product is able to free itself from the catalyst surface more readily and make the site competitively available sooner to either more **3** or cyclohexene. This accounts for the increased overall rate of hydrogenation, relative to **11**, as evidenced by the lower hydrogen pressure required for reaction.

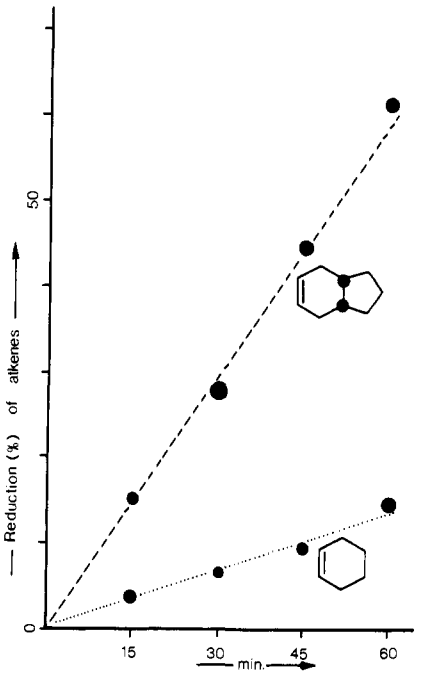


Figure 1. The competitive reduction of *cis*-bicyclo[4.3.0]non-3-ene and cyclohexene.

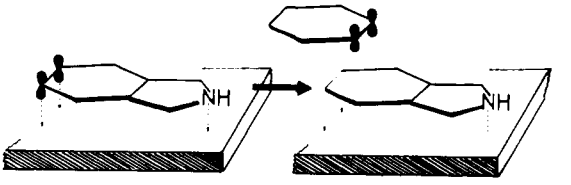


Figure 2. Steric hindrance during catalytic reduction.

Rationalization for the reactivity of **9** is more difficult. Greater molecular bulk would demand that these molecules, as an adsorbed layer, would sterically block more sites than a smaller molecule. Also, having greater van der Waals attractive forces, due to the larger number of atoms in **9** relative to cyclohexene, might be invoked as one of the important differences. Assuming that bulk sizes of **3**, **9**, and **11** are about the same, it is tempting to ascribe reactivity differences in the series to the heteroatom-catalyst interactions.

At this juncture it is appropriate to state that rationalizations invoking molecular bulk as controlling the behavior of **9** require some inherent and probably inseparable differences in molecules of the bicyclic series and cyclohexene. This difference is, in an oversimplification, represented by the factor for **9** (4.92). Thus, since **3** and **11** have heteroatom plus van der Waals interactions, while **9** has only the latter, it might be considered that 4.92 represents some minimum difference on reactivity between this system and cyclohexene, and that any member of the bicyclic series might be expected to hydrogenate faster than cyclohexene by at least 4.92. Using this factor we can normalize the Table I relative ratios to **3** (1.33); **9** (1.00); **11** (4.80). Thus the differences in reactivity can still be ascribed to a heteroatom-catalyst interaction.

An experiment was initiated to test this. Equal molar amounts of an alkene (either **3**, **9**, or **11**) and cyclohexene were mixed with ethanol and catalyst. The amount of catalyst was substantially increased over that used in the hydrogenation experiments. The mixtures were shaken for 10 min in the absence of hydrogen, after which time the amounts of unadsorbed cyclohexene and alkene were quantitatively determined. Each analysis was performed three times, and the decrease in the amount of substrates was taken as indicative of how much was adsorbed to the catalyst.

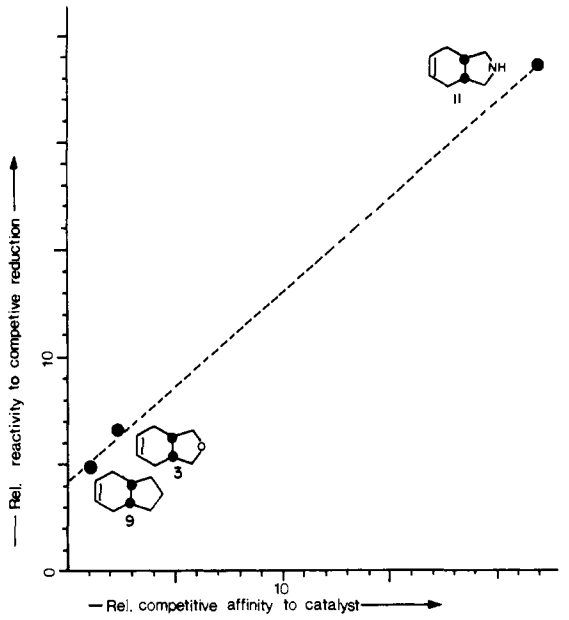


Figure 3. Correlation of competitive reduction and competitive affinity to catalyst.

$$S + C \rightleftarrows S\text{-}C$$

where S = substrate, C = catalyst, and S-C = substrate-catalyst complex.

$$K_{EQ} = \frac{[S - C]}{[S][C]} \approx \frac{[S_0] - [S_t]}{[S_t]}$$

where $[S_0]$ and $[S_t]$ are the concentrations measured at the start of the experiment and after 10 min, respectively. Since the catalyst is not in solution, its concentration is not included in the final expression. The results of these experiments are summarized in Table II. The competitive reductions and affinity studies are shown to correlate very well (Figure 3), and help substantiate the notion that the heteroatom-catalyst interaction is very important.

At this juncture we have suggested that the heteroatom-platinum complex is responsible for fast reductions of **3** and **11** relative to cyclohexene. Bulk effects can be suggested for **9**. Conversely, we must not eliminate the rationalization that because of the inability of cyclohexene to find free catalyst sites competitively we are observing decreased reactivity of cyclohexene. A test for this was possible in a noncompetitive experiment. Each alkene was placed in a separate test tube with ethanol and catalyst. A series of the test tubes was placed in the Parr hydrogenation flask, as in the previous competition experiments. After 20 min at 20 psi hydrogen pressure, the contents of each test tube were examined by quantitative GLC. This experiment utilized the same ratios of alkene, solvent, catalyst, and the same hydrogen pressure, temperature, and time as in the competitive experiment, but eliminated the actual competitive interferences of one molecule with another. The results of these studies, normalized to cyclohexene, are summarized in Table III.

These results are consistent with the concept of heteroatom interactions with the catalyst sites, in suggesting that cyclohexene is more reactive than any of the other alkenes because its turnover rate is greater. There seems to be a problem relative to **3** and **9**, however, in that the magnitudes are in reverse order from the competitive hydrogenations. Here we may be seeing the effects of the oxygenated solvent playing a role. The attraction of oxygen for the platinum makes **3** more competitive to the sites than **9**, since it is possible that the site exchange of ether oxygen for alcohol oxygen is more favorable than alkene bond for alcohol oxygen. This gives a better probability that the alkene bonds of **3** will be in better position than the similar bonds of **9**.

Table II. Competitive Catalyst Affinity Studies

	3 (O)	**9** (CH_2)	**11** (NH)
K compd/K cyclohexene	2.3	0.9	22

Table III. Noncompetitive Hydrogenations

	cyclohexene	**3** (O)	**9** (CH_2)	**11** (NH)
rel rate[a]	1.00	0.78 ± 0.003	0.13 ± 0.004	0.004 ± 0.002

[a] Normalized to cyclohexene.

Support for this can be seen by comparison of the noncompetitive adsorption studies (carried out in the same fashion as the competitive adsorption studies) with the noncompetitive reactivities (Figure 4). These results demonstrate that there is a relationship between adsorption on the catalyst and reactivity, and even in this analysis the trends of reactivity and adsorptivity of **3** and **9** are maintained. We do not, at this time, know the reasons for the differences in trends for **3** and **9** in the competitive and noncompetitive reactions; however, work will continue toward answering this question.

In conclusion, we have, in a structurally homogeneous series, initiated the development of a quantitative basis for examining heteroatom assistance or poisoning (depending on whether the heteroatom is part of the molecule being reduced or from another source, respectively). This work may find extensions in rationalizing specificities associated with certain functional groups in various catalytic processes.

Experimental Section

Boiling and melting points are uncorrected. Infrared spectra were obtained from a Beckman IR-5 instrument. NMR spectra were recorded on a Varian A-60 instrument, using Me_4Si as internal standard. Chemical shifts are reported in parts per million, relative to Me_4Si. Gas chromatographic analyses were performed using a Varian Aerograph Series 1400 instrument with thermal conductivity detectors. Chromatogram areas were obtained using a Minigrator electronic integrator. Physical and spectral data for compounds previously reported were compared to the literature values. Sample integrity was ensured by GLC analysis. Samples were purified by distillation and/or chromatographic methods to homogeneity.[16]

Detector Calibration. Carefully weighed ethanolic solutions containing equal molar amounts of cyclohexene/cyclohexane and **3**/**17** were used to examine detector responses to two-proton differences. From each mixture six injections were made into the gas-liquid chromatograph, and the chromatogram peak areas were determined by electronic integration. The results are listed below.

Cyclohexane/Cyclohexene. Analysis was performed using a 12.5 ft by ⅛ in. copper column, filled with 15% SE-30 on acid-washed Chromosorb W (80–100 mesh). Column temperature was maintained at 90 °C with helium flow rate of 22 cm³/min. % of each component: cyclohexane/cyclohexene = 50.48/49.52 ± 0.10.

17/3. Analysis was performed using a 15 ft by ⅛ in. copper column, filled with 15% Carbowax 20M on 10% KOH-washed Chromosorb W (60–80 mesh). Column temperature was 180 °C and helium flow rate was 30 cm³/min. % of each component: **17**/**3** = 50.24/49.70 ± 0.15.

Sample Size Calibration. In order to know whether the sample size of the injection would not alter the GLC data, a cyclohexane/cyclohexene sample was prepared. Four injections for each sample size were measured for uniformity of peak area (Table IV).

Temperature Calibration to Response. Four 1.0-μL injections of the same sample were made at different temperatures. The results are tabulated in Table V.

Preparation of *cis*-1,2,3,6-Tetrahydrophthalyl Alcohol (2).[2] A solution of *cis*-1,2,3,6-tetrahydrophthalic anhydride (**1**, 152 g, 1.0 mol) in 800 mL of dry THF was added dropwise to a stirring mixture of $LiAlH_4$ (43.7 g, 1.15 mol) in 250 mL of dry THF. After the addition

Table IV.

sample size, μL	cyclohexane/cyclohexene	*S*
0.5	58.33/41.67	±0.24
1.0	58.29/41.71	±0.17
2.0	58.33/41.67	±0.14
3.0	58.54/41.46	±0.03
4.0	58.64/41.36	±0.10
5.0	58.93/41.07	±0.08
av	58.51/41.49	±0.26

Table V.

temp, °C	cyclohexane/cyclohexene	*S*
40	58/86/41.14	±0.17
50	58.63/41.37	±0.25
60	58.47/41.53	±0.08
70	58.18/41.82	±0.54
av	58.53/41.47	

was complete, the mixture was refluxed for 24 h. It was then hydrolyzed by the dropwise addition of a saturated Rochelle salt solution until it turned white. The mixture was refluxed for an additional 10 h, allowed to cool to room temperature, and suction filtered. The solvent was removed and the viscous liquid was distilled to give the colorless diol (117.7 g, 82% yield): bp 110-111 °C (0.25 mm) (lit.[2] bp 165-170 °C (12 mm)); NMR 1.83 (sharp s, 6 H), 3.18 (m, 4 H), 3.71 (sharp s, 2 H), 4.94 ppm (t, 2 H).

Preparation of *cis*-8-Oxabicyclo[4.3.0]non-3-ene (3).[3] A solution of tosyl chloride (24.7 g, 0.13 mol) in 35 mL of pyridine was added dropwise to a refluxing solution of **2** (15.0 g, 0.11 mol) in 25 mL of pyridine. When the addition was complete, the mixture was refluxed for 4 h. The solution was cooled to room temperature and poured into a H_2SO_4 ice bath to neutralize the pyridine. The mixture was then extracted with Et_2O. The extracts were dried over anhydrous $MgSO_4$ and stripped of solvent, and the crude product was distilled, resulting in 8.9 g of the colorless *cis*-8-oxabicyclo[4.3.0]non-3-ene (58% yield): bp 90-93 °C (18 mm) (lit.[3] bp 63-64 °C (13 mm)); NMR 2.15 (methylene envelope, 4 H), 2.41 (2 H), 3.52 (q, 2 H), 3.88 (q, 2 H), 5.67 ppm (t, 2 H); ^{13}C NMR 36.359 (2 C), 47.580 (2 C), 85.235 (2 C), 137.132 ppm (2 C).

Preparation of *cis*-1,2,3,6-Tetrahydrophthalyl Alcohol Di-*p*-toluenesulfonate (5). A solution of **2** (65.6 g, 0.46 mol) in 200 mL of pyridine was added dropwise to a stirred solution of tosyl chloride (260.9 g, 1.37 mol) in 400 mL of pyridine at 0 °C. The mixture was stirred at 0 °C for 3 h and then poured into 800 mL of ice water. The solid which formed was collected by suction filtration and recrystallized from MeOH. The white, crystalline ditosylate was obtained (157.3 g, 75.7% yield): mp 97-98 °C (lit.[2] mp 96 °C); NMR 1.95 (broad, 4 H), 2.25 (2 H), 2.41 (sharp s, 6 H), 3.98 (d, 4 H), 5.45 (t, 2 H), 7.55 ppm (d of d, 8 H).

Preparation of *cis*-8-Thiabicyclo[4.3.0]non-3-ene (4).[4] A solution containing 43.0 g (0.096 mol) of **5** and 31.2 g (0.13 mol) of $Na_2S \cdot 9H_2O$ in 500 mL of 95% EtOH was refluxed for 17 h. The reaction mixture was worked up by distilling off the EtOH and extracting the product with Et_2O. The solvent was removed and the residue was distilled, resulting in 4.45 g of the colorless sulfide (33.3% yield): bp 121-125 °C (10 mm); infrared 3020, 2900, 2860, 2840, 1655, 1450, 1430, 1260, 1200, 945, and 650 cm^{-1}; NMR 2.41 (methylene envelope, 4 H), 2.42 (2 H), 2.75 (m, 4 H), 5.57 ppm (t, 2 H); ^{13}C NMR 38.140 (2 C), 48.120 (2 C), 51.950 (2 C), 136.916 ppm (2 C). Anal. Calcd for $C_8H_{12}S$: C, 68.57; H, 22.85; S, 8.58. Found: C, 68.43; H, 22.79; S, 8.57.

Preparation of Cyclohexene-4-*cis*-1,2-diacetonitrile (6).[5] A mixture of **5** (110 g, 0.244 mol), NaCN (36 g, 0.735 mol), and EtOH (700 mL) was refluxed for 60 h in a 2-L round-bottom flask equipped with a condenser and mechanical stirrer. When the reflux period had ended and the reaction mixture had cooled, 200 mL of water was added to dissolve the salts. The EtOH was removed by distillation, and, after cooling, the remaining brown liquid was seeded with a few dust particles to yield white needles. After these were collected by suction, addition of ice water to the filtrate and cooling gave additional crystals. The crops were combined to yield 39.1 g (75.7%) of the dinitrile: mp 47-50 °C (lit.[52] 50 °C); NMR 2.20 (broad m, 6 H), 2.48 (d, 4 H), 5.64 ppm (t, 2 H).

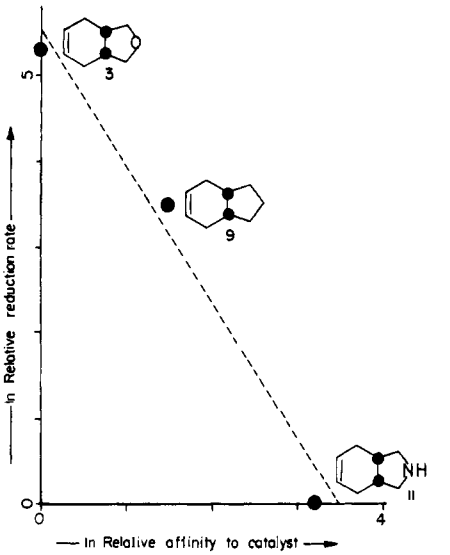


Figure 4. Correlation of noncompetitive reduction and noncompetitive catalyst affinity.

Preparation of Cyclohexene-4-*cis*-1,2-diacetic Acid (7).[5] A solution of 28.35 g (0.18 mol) of **6** and 125 mL of 33% aqueous KOH was refluxed until the evolution of ammonia had ceased (approximately 21 h). The reaction mixture was acidified in an ice bath with 125 mL of 85% H_3PO_4, liberating the organic diacid and inorganic salts. The solid was collected by filtration, and the inorganic salts were dissolved in hot water, leaving the diacid behind. The diacid was recrystallized from MeOH, yielding 13.35 g (38.1%) of product: mp 157-159 °C (lit.[5] mp 157 °C); NMR 2.07 (m, 4 H), 2.28 (2, 6 H), 5.58 (t, 2 H), 9.10 ppm (2 H).

Preparation of *cis*-Bicyclo[4.3.0]non-3-en-8-one (8).[5] **7** (13.0 g, 0.066 mol), 1.9 g of $Ba(OH)_2 \cdot 8H_2O$, and 13.0 g of iron powder were thoroughly mixed in a round-bottom flask and heated with an open flame. The ketone was separated from the water, which codistilled and was redistilled to yield 5.7 g (63.8%) of the yellow-colored ketone: bp 115-118 °C (13 mm) (lit.[2b] bp 110-115 °C (12 mm)); NMR 2.10 (methylene envelope, 8 H), 2.40 (2 H), 5.60 ppm (t, 2 H).

Preparation of *cis*-8-Azabicyclo[4.3.0]non-3-ene (11).[1d] A solution of *cis*-1,2,3,6-tetrahydrophthalimide (**10**, 40.0 g, 0.27 mol) in 300 mL of dry THF was added dropwise to a stirring mixture of $LiAlH_4$ (11.4 g, 0.3 mol) in 200 mL of dry THF in a nitrogen atmosphere. When the addition was complete, the mixture was allowed to reflux for 7 h. At the end of the reflux period, the reaction mixture was cooled to room temperature and a saturated Rochelle salt solution was added until no further reaction was noted. The mixture was then suction filtered, the solvent removed, and the residue distilled, resulting in 15.0 g (45%) of the colorless amine: bp 86-92 °C (10 mm) (lit.[1d] bp 77-80 °C (10 mm)); NMR 2.04 (6 H), 2.70 (4 H), 3.03 (1 H), 5.63 ppm (t, 2 H); ^{13}C NMR 37.277 (2 C), 47.796 (2 C), 62.250 (2 C), 137.455 ppm (2 C).

Preparation of *trans*-Diethyl 1,2,3,6-Tetrahydrophthalate (14). The Diels-Alder reaction was carried out by bubbling 29 g (0.37 mol) of butadiene into a solution of 53.05 g (0.31 mol) of diethyl fumarate in 200 mL of benzene at 0 °C and heating the mixture in a bomb at 50 °C for 24 h. The benzene was removed and the product distilled to yield 29.2 g (42%) of the colorless diester: bp 115-117 °C (1.6 mm) (lit.[14] bp 109-111 °C (0.5 mm)); NMR 1.19 (t, 6 H), 2.27 (broad, 4 H), 2.67 (m, 2 H), 4.05 (q, 4 H), 5.63 ppm (2 H).

Preparation of *trans*-1,2,3,6-Tetrahydrophthalyl Alcohol (15).[2] A solution of 28.6 g (0.127 mol) of *trans*-diethyl 1,2,3,6-tetrahydrophthalate in 150 mL of dry THF was added dropwise, with stirring, to 6.0 g (0.16 mol) of $LiAlH_4$ in 150 mL of THF. The mixture was refluxed for 12 h, cooled to room temperature, and hydrolyzed with 30 mL of saturated Rochelle salt solution. The mixture was refluxed for an additional 4 h, cooled, and filtered, and the solvent was removed. Distillation resulted in 15.25 g (85% yield) of the diol: bp 105-107 °C (0.25 mm) (lit.[2] bp 162-165 °C (12 mm)); NMR 1.90 (6 H), 3.50 (4 H), 5.09 (2 H), 5.52 ppm (2 H).

Preparation of *trans*-8-Oxabicyclo[4.3.0]non-3-ene (16).[15] A solution of 10.0 g (0.053 mol) of tosyl chloride in 30 mL of pyridine was added dropwise to a refluxing solution of 5.5 g (0.039 mol) of **15** in

30 mL of pyridine. The mixture was refluxed for 8 h, cooled to room temperature, poured into ice water, and acidified with concentrated HCl. The product was extracted with Et_2O and dried over anhydrous $MgSO_4$, and the solvent was removed. Distillation of the residue resulted in 3.4 g (70.8% yield) of the colorless bicyclic ether: bp 82–84 °C (15 mm) (lit.[15] bp 77–78 °C (18 mm)); NMR 1.87 (6 H), 3.20 (t, 2 H), 3.88 (q, 2 H), 5.67 ppm (2 H).

Preparation of *cis*-8-Oxabicyclo[4.3.0]nonane (17).[4] A solution of 7.0 g (0.45 mol) of *cis*-1,2-cyclohexanedicarboxylic anhydride in 50 mL of dry THF was added to 2.5 g (0.065 mol) of $LiAlH_4$ in 50 mL of dry THF. When the addition was complete, the mixture was refluxed for 24 h. The reaction mixture was then cooled to room temperature and hydrolyzed with 10 mL of saturated Rochelle salt solution. The mixture was refluxed for an additional 7 h, cooled, then filtered. The solvent was removed and the viscous liquid was distilled, yielding 5.85 g (89.4%) of the clear cis diol: bp 110–112 °C (0.6 mm) (lit.[13] bp 134–136 °C (3 mm)); NMR 1.44 (8 H), 1.82 (2 H), 3.50 (4 H), 5.00 ppm (2 H).

A solution of 4.5 g (0.024 mol) of tosyl chloride in 30 mL of pyridine was added to a refluxing solution of 2.5 g (0.017 mol) of *cis*-1,2-di(hydroxymethyl)cyclohexane, prepared in 20 mL of pyridine. The mixture was refluxed for 12 h, cooled, and poured into 100 mL of ice water. The solution was slightly acidified with concentrated HCl and the product was extracted with Et_2O. The extracts were dried over anhydrous $MgSO_4$. The solvent was removed and the residue was distilled to yield 1.65 g (73.3%) of the desired product: bp 98–99 °C (40 mm) (lit.[4] bp 180 °C); NMR 1.45 (8 H), 2.12 (2 H), 3.56 ppm (4 H).

Preparation of *trans*-8-Oxabicyclo[4.3.0]nonane (18).[4] The same procedure was followed as in the preparation of *cis*-1,2-di(hydroxymethyl)cyclohexane using 5.8 g (0.038 mol) of *trans*-1,2-cyclohexanedicarboxylic anhydride and 2.4 g (0.058 mol) of $LiAlH_4$. Distillation resulted in 3.65 g (75.1% yield) of the clear trans diol: bp 109–110 °C (0.65 mm) (lit.[13] bp 120 °C (2 mm)); NMR 1.25 (8 H), 1.80 (2 H), 3.52 (4 H), 4.40 ppm (2 H).

The same procedure was used as in the preparation of **17**. The diol prepared above (2.5 g) and 4.5 g (0.024 mol) of tosyl chloride were reacted as previously described. Distillation resulted in 1.25 g of the product (57.1% yield): bp 95–97 °C (38 mm) (lit.[4] bp 80 °C (31 mm)); NMR 1.27 (6 H), 1.83 (4 H), 3.14 (2 H), 3.77 ppm (2 H).

Competitive Hydrogenation with 5% Pt/Alumina. Each substrate (cyclohexene and its bicyclic competitor) (0.001 mol), 1.0 mL of absolute EtOH, and 0.0025 g of 5% Pt/alumina were placed in each of several 3-in. test tubes. The test tubes were placed in a hydrogenation flask of a Parr hydrogenation apparatus; hydrogen was introduced, and the mixtures were hydrogenated for 30 min with constant shaking at 20 psi at 20 °C. The product distribution relative to the starting materials was analyzed by gas chromatography. Reactions involving **4** or **11** required 60 and 40 psi hydrogen pressure, respectively. All competitions were repeated in triplicate.

In the competitive hydrogenations, the following average percent reductions were observed: (cyclohexene), 6; (**3**), 32. (cyclohexene), 28; (**9**), 7. (cyclohexene), 4; (**16**), 4. (cyclohexene), 1; (**11**), 13.

Noncompetitive Hydrogenation. Equimolar amounts (0.001 00 mol) of cyclohexene and the bicyclic compounds **3**, **9**, **11**, and **16** were independently placed in separate test tubes. Equivalent amounts of 100% EtOH (1.0 mL) and 5% Pt/alumina (0.002 55 g) were added to each test tube. As many samples as could fit in the hydrogenation flask were hydrogenated at one time, with shaking, for 20 min at 20 psi. Where multiple runs were necessary, new cyclohexene standards were hydrogenated, along with the samples, at 20 °C.

In the noncompetitive hydrogenations, the following average percent reductions were observed: (cyclohexene), 26; (**3**), 22. (cyclohexene), 27; (**9**), 4. (cyclohexene), 25; (**16**), 15. (cyclohexene), 32; (**11**), 0.15.

Competitive Catalyst Affinity. Equimolar quantities (2.56×10^{-5} mol) of the alkenes **3**, **9**, and **11** were paired in test tubes with an equal quantity of cyclohexene to which 0.100 g of 5% Pt/alumina and 0.5 mL of 100% EtOH were added. The samples were shaken in the absence of H_2 for 20 min at 20 °C. The decrease in concentration of each component, as determined by GLC monitoring, was interpreted to reflect the affinity of each component for the catalyst, relative to cyclohexene.

Noncompetitive Catalyst Affinity. Equimolar quantities (2.56×10^{-5} mol) of the alkenes **3**, **9**, and **11** and cyclohexene were placed individually in test tubes, along with 0.100 g of 5% Pt/alumina and 0.5 mL of 100% EtOH. Equilibration and concentration monitoring were performed by the same method as in the competitive catalyst affinity experiment.

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