concentration of solute molecules on the pitch of the cholesteric solvent, it should be possible to increase the rates and specificities of some reactions, decrease the rates, and redirect the stereochemical courses of others. We shall report such examples in future publications.

Acknowledgment. We thank Drs. Wolfgang Elser and Daniel Martire for helpful discussions concerning this work. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, to The National Science Foundation (Grant No. CHE76-84120), and to the Naval Research Laboratory (Grant No. N00173-77-C-0077) for support of this research.

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(5) (a) I. Hartmann, W. Hartmann, and G. O. Schenck, *Chem. Ber.*, **100**, 3146 (1967); (b) R. Livingston and K. S. Wei, *J. Phys. Chem.*, **71**, 541 (1967).
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(7) Syn/anti product ratios were not calculated in experiments carried to 10–15% conversions of acenaphthylene: overlap of the ultraviolet spectra of the monomer with both dimers precludes an accurate determination of either dimer independently. Small changes in the total optical density at a given wavelength result in large variations in the calculated product ratio. Under our irradiation conditions, the dimers neither interconvert nor reconvert to acenaphthylene.
(8) The cholestanyl mixture, mp 71–72 °C, exhibits a monotropic liquid crystalline phase from 54 to <10 °C. It was utilized here owing to its thermal and photochemical stability. The complete phase diagram will be reported in a full paper.
(9) The details of the experimental procedure and spectral data on starting materials and products will be reported in a full paper.
(10) Nitrogen-saturated toluene solutions of acenaphthylene were irradiated in duplicate in a merry-go-round apparatus with a 450-W medium-pressure mercury arc using Corning No. CS-054 and CS-737 filters. Ferrioxalate solutions at 25 °C were employed as the actinometers.
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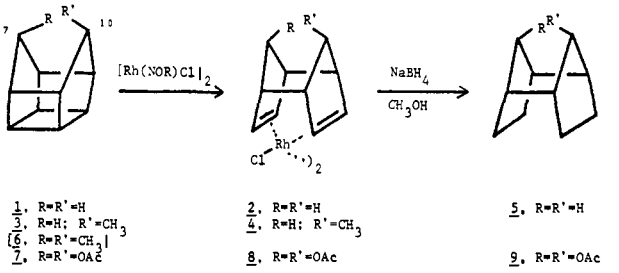
Long-Range Steric Effects in Rhodium(I) Cleavages of Secopentaprismanes. A Reversible Rhodium(I)-Mediated Cyclobutane–Diolefin Conversion[1]

Sir:

We have found that rhodium(I) complexes of *syn*-tricyclo[4.2.1.$1^{2,5}$]deca-3,7-dienes can be prepared readily by rhodium(I)-induced cleavage[2] of the strained secopentaprismane cage system.[3] Thus, secopentaprismane (**1**, mp 108–109 °C) reacts with an equivalent of $[Rh(NOR)Cl]_2$ in chloroform at 70 °C to give **2** and free norbornadiene. The structure of the ligand in **2**, as drawn, is fully consistent with the NMR spectra of the complex: ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.26 (4 H, br s), 2.65 (4 H, br s), 1.65 (2 H, d, J = 12 Hz), 1.34 ppm (2 H, d, J =12 Hz); ^{13}C NMR (22.63 MHz, proton decoupled, Me_2SO-d_6) δ 88.0 (4 C, J_{Rh-C} = 15 Hz), 45.0 (4 C), 43.3 ppm (2 C, J_{Rh-C} = 3 Hz). Similarly, the reaction of 7-*endo*-methylsecopentaprismane (**3**) with $[Rh(NOR)Cl]_2$ was shown to give the diene complex **4**.[4]



1, R=R'=H
3, R=H; R'=CH_3
6, R=R'=CH_3
7, R=R'=OAc

2, R=R'=H
4, R=H; R'=CH_3
8, R=R'=OAc

5, R=R'=H
9, R=R'=OAc

Complexes **2** and **4** are quite stable. The diene ligand is not displaced by CO, phosphines, or norbornadiene at a useful rate. As the metal is ligated tightly, the cleavage reaction is not catalytic in rhodium(I), unlike the related reactions of cubane[2a] and homopentaprismane.[2c] The complexes are reduced readily by sodium borohydride in methanol;[5] for example, reduction of **2** gives rhodium metal and *syn*-tricyclo[4.2.1.$1^{2,5}$]decane (**5**) in nearly quantitative yield: ^{1}H NMR δ 2.28 (4 H, br s), 1.77, 1.69 (6 H, centers of overlapping multiplets), 1.18 (4 H, br d), 0.45 ppm (2 H, br d); ^{13}C NMR ($CDCl_3$) δ 36.0, 29.6, 25.7 ppm.[6] The cleavage and reduction reactions are quite general and offer special synthetic opportunities; access to the *syn*-tricyclo[4.2.1.$1^{2,5}$]decane system is otherwise very limited.[7] In this communication, however, our concern is with the extraordinary effects of methano bridge substituents on the reactivity of the secopentaprismanes and the related complexes.

The rates of cleavage of **1** and **3** by an equivalent of Rh(NOR)acac[8] in $CDCl_3$ at 50 °C were measured by standard ^{1}H NMR techniques. Both reactions appear cleanly second order to at least 90% completion: for **1**, $k_2 = 1.3 \times 10^{-2}$ L mol^{-1} s^{-1}; for **3**, $k_2 = 1.3 \times 10^{-3}$ L mol^{-1} s^{-1}. The tenfold decrease in second-order rate constant resulting from the introduction of a methyl group well away from the reaction site is remarkable. Even more so is the fact that introduction of a second *endo*-methyl group stops the reaction altogether; we cannot detect reaction of 7-*endo*,10-*endo*-dimethylsecopentaprismane (**6**, mp 88–89 °C) with Rh(NOR)acac even under conditions more severe than those used for the cleavage of **1** and **3**.

We suggest that the effect of *endo*-methyl groups so far from the site of ring cleavage arises in steric interference to the intranuclear movements which accompany opening of the cage. The bridgehead atoms, C-1, C-6, C-8, and C-9, act as pivots transmitting movement within these fairly rigid molecules. The moving apart of C-2, C-5 and C-3, C-4 that must occur as the cage cyclobutane rings are broken results, via these pivots, in the methano bridges (and their endo substituents) moving toward one another. This becomes energetically more difficult as the endo substituents increase in number and/or effective size. Apparently, steric compression would become so severe in the *endo*-dimethyl case that even the great exothermicity of the cage cleavage is insufficient to drive the reaction significantly forward.[9]

Such long-range steric effects probably also account for the lack of reactivity of diene complexes like **2** and **4** in ligand exchange reactions. We suspect that, if the diene were to come free of the metal, steric compression at the methano bridges would increase. Again the point being that energetically favorable increases in distance (d) between C-2, C-5 and C-3, C-4 engender, by way of the bridgehead pivot atoms, unfavorable decreases (d′) between the atoms on the methano bridges.[10]

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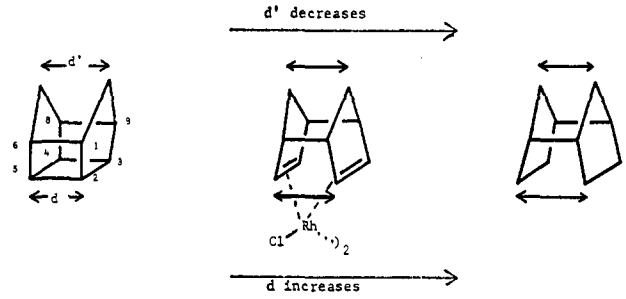
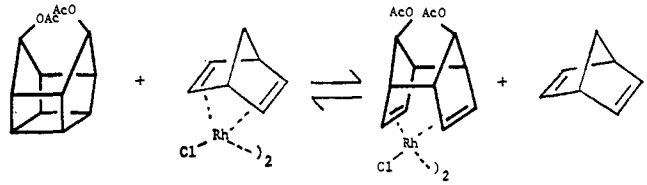
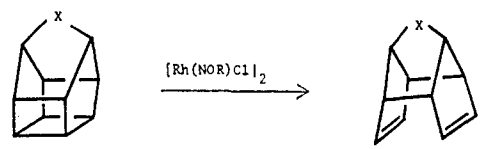


The endo diacetate **7** (mp 116–117 °C) behaves, in one way, like its relatives **1** and **3**; that is, it is cleaved by an equivalent of $[Rh(NOR)Cl]_2$ to diene complex **8**, identified by NMR analysis (^1H NMR 4.75 (4 H, br s), 4.10 (2 H, br s), 3.05 (4 H, br s), 2.00 ppm (6 H, s); ^{13}C NMR 169.8, 78.9 (d, J_{Rh-C} = 16 Hz), 71.9 (d, J_{Rh-C} = 5 Hz), 46.7, 21.1 ppm) and by reduction with sodium borohydride in methanol to **9** (mp 125–126 °C; ^1H NMR δ 4.28 (2 H, br s), 2.52 (4 H, br s), 2.11 (6 H, s), 1.82–1.69 (4 H, m), 1.53–1.43 ppm (4 H, m); ^{13}C NMR δ (carbonyl not observed) 73.6, 36.9, 23.4, 21.7 ppm). Remarkably, and we believe without precedent,[11] treatment of **8** with excess norbornadiene *reverses the rhodium(I) cyclobutane-diolefin cleavage reaction and regenerates the cage secopentaprismane.* Apparently, we have here a case in which the energy changes associated with the strain release and rebonding that come with cleavage of the cage are of the same magnitude, but opposite in sign, as those changes in nonbonding interactions that must also accompany the process. In this fortuitous circumstance we can see operationally changes in the position of equilibrium with changes in the concentration of the norbornadiene component. A quantitative examination of this equilibrium cleavage–closure reaction awaits further effort.



7 **8**

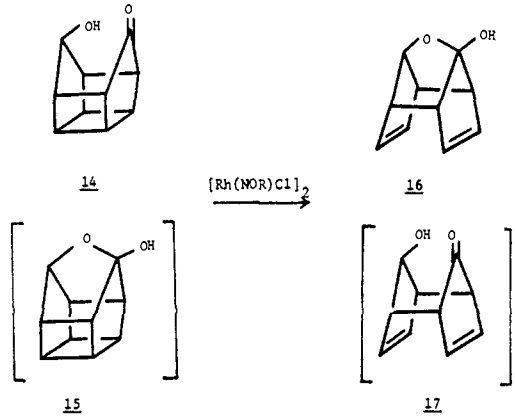
If the steric effects destabilizing the diene ligands in complexes like **2, 4,** and **8** were removed, it follows from our arguments that ligand exchange with norbornadiene would occur, the diene would be freed, $[Rh(NOR)Cl]_2$ would be regenerated, and the parent secopentaprismane would be cleaved catalytically. Indeed, the "bridged secopentaprismanes" oxahomopentaprismane (**10,** mp 171–172 °C) and homopentaprismane (**11**)[2c] are cleaved easily and catalytically by $[Rh(NOR)Cl]_2$ to the free dienes **12** and **13,** respectively. In these cases, the nonbonded interactions destabilizing the free ligands of **2, 4,** and **8** have been removed, in effect, by bonding the offending groups together.



10, X=O
11, X=CH_2

12, X=O
13, X=CH_2

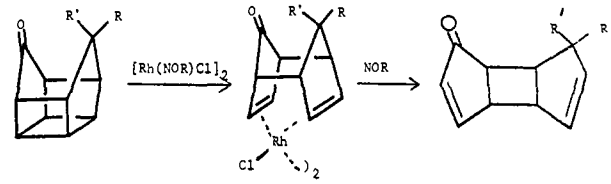
Secopentaprismane **14** (mp 230–231 °C) provides a related illustration. This hydroxy ketone exists, as shown by IR spectroscopy, primarily in the open form and not as the corresponding bridged hemiketal **15**. $[Rh(NOR)Cl]_2$ effects ready catalytic cleavage of **14**/**15**. Unlike the cage starting material, the diene product (mp 193–194 °C) exists primarily as the bridged hemiketal **16** and not as the corresponding hydroxy ketone **17**. The unmistakeable shift in the positions of equilibrium provides a good operational demonstration that a change in distance between the one-carbon bridges does accompany cleavage of the cage.



14 **16**

15 **17**

In other cases, ketone groups even more markedly alter the outcome of the rhodium(I) cleavage of secopentaprismanes. We have found that ketones **18a–c** react quantitatively with catalytic amounts of $[Rh(NOR)Cl]_2$ to produce the conjugated ketones **20a–c,** respectively, derivatives of the unexpected *cis,syn,cis*-tricyclo[5.3.0.$0^{2,6}$]deca-3,9-diene system.[12] We now know that these reactions (at least those of **18a** and **18b**) proceed by way of rhodium complexes of the expected *syn*-tricyclo[4.2.1.$1^{2,5}$]deca-3,7-diene system, as in the cleavages of **1, 3,** and **7**. Complexes **19a** and **19b** have been isolated and characterized fully; ^{13}C NMR spectroscopy unambiguously differentiates the ring systems in question.[13] These complexes are stable in the absence of norbornadiene, but react with it readily to give $[Rh(NOR)Cl]_2$ and **20a** or **20b,** as appropriate. A number of interesting possibilities can be suggested to account for the skeletal rebonding that must occur during the transformation **19** → **20** (e.g, very rapid Cope rearrangement, cage reclosure–reopening, etc.). We are working now to sort these out experimentally.



18a, R=R'=OCH_3
18b, R=H, R'=CH_3
18c, R,R' = =O

19a–c **20a–c**

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References and Notes

(1) Taken in part from the Ph.D. Thesis of Dennis R. Patterson, The University of Chicago, 1974.
(2) See, for examples, (a) L. Cassar, P. e. Eaton and J. Halpern, *J. Am. Chem. Soc.*, **92**, 3515 (1970); (b) W. C. Dauben and A. J. Kielbania, Jr., *ibid.*, **93**, 345 (1971); (c) P. E. Eaton, L. Cassar, R. A. Hudson and D. R. Hwang, *J. Org. Chem.*, **41**, 1445 (1976).
(3) The new secopentaprismanes made for this study were synthesized in straightforward fashion from dione **18c**, which can be prepared in moderate

yield as described by J. C. Barborak, L. Watts, and R. Pettit, *J. Am. Chem. Soc.*, **88**, 1328 (1966), and J. C. McKennis, L. Brener, J. S. Ward, and R. Pettit, *ibid.*, **93**, 4957 (1971). Each new compound was characterized appropriately.

(4) The chloro-bridged dimeric structure of these compounds is assumed based on the usual behavior of RhCl–diene complexes. In all probability the bridge is disrupted in Me_2SO.

(5) To our knowledge, this is the first application of this reduction method to rhodium–diene complexes. It proceeds readily in good yield, apparently via σ-bonded intermediates. Saturation of the olefin bonds is intrinsic to the process. The presence of the halogen (and/or the halogen bridge) seems essential, for monomeric acetylacetonate rhodium–diene complexes are reported not to be reduced by sodium borohydride (B. R. G. Johnson, H. V. P. Jones, and J. Lewis, *J. Chem. Soc., Dalton Trans.*, 463 (1972)). We shall consider the mechanism of this reduction in a later paper.

(6) This compound has just recently been prepared by L. A. Paquette and coworkers using a totally different route.[7a]

(7) (a) L. A. Paquette, G. Klein, and C. W. Doecke, *J. Am. Chem. Soc.*, **100**, 1595 (1978); (b) I. A. Akhtar, G. I. Fray, and J. M. Yarrow, *J. Chem. Soc. C*, 812 (1968).

(8) Prepared by stirring $[Rh(NOR)Cl]_2$ with acetylacetone and sodium carbonate in aqueous THF at room temperature, followed by extraction into chloroform and crystallization from methylene chloride; cf. the original, but poorer yield route of F. Bonati and G. Wilkinson, *J. Chem. Soc.*, 3156 (1964). The complexes resulting from reaction of Rh(NOR)acac with **1** and **3** are highly crystalline, mp 142–143 and 90–92 °C, respectively. The NMR spectra closely resemble those of **2** and **4**. The acetonylacetonate complexes (monomeric) are more soluble than the chloro complexes (bridged dimers) and hence better suited for kinetic measurements.

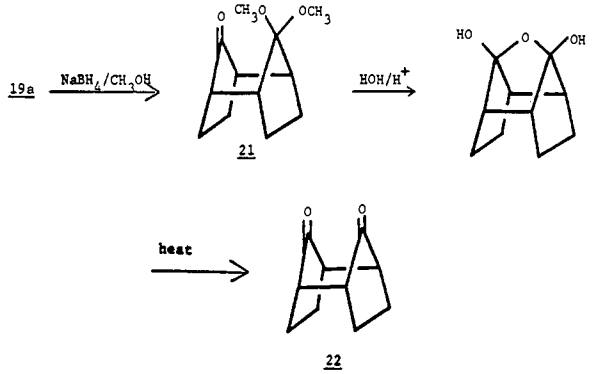
(9) The *endo*-methyl groups are already badly compressed in **6**; $J_{^{13}C-H}$ at the methano bridge is 119 Hz.

(10) The effects of steric compression are clearly evident in the NMR spectra and reactions of the free diene; see C. W. Doecke, G. Klein, and L. A. Paquette, *J. Am. Chem. Soc.*, **100**, 1596 (1978).

(11) An important, related observation has been reported by P. G. Gassman and T. H. Johnson, *J. Am. Chem. Soc.*, **98**, 861 (1976), which see.

(12) P. E. Eaton and C. A. Cerefice, *Chem. Commun.*, 1494 (1970).

(13) Furthermore, sodium borohydride reduction gives the corresponding saturated *syn*-tricyclo[4.2.1.$1^{2,5}$]decane free of rhodium. Thus, for example, **19a** is reduced to **21** (mp 98–99 °C) quantitatively. (Note that the ketone



21 22

group survives; apparently the rhodium black catalyzed reaction of $NaBH_4$ with methanol is much faster than $NaBH_4$ reduction of the ketone.) Hydrolysis of **21** and subsequent desiccation gives dione **22** of C_{2v} symmetry: IR (CCl_4) ν 1770 cm^{-1}; ^1H NMR δ 2.44–2.16 (8 H), 1.89–1.61 ppm (4 H); ^{13}C NMR δ 212.6, 45.7, 18.7 ppm.

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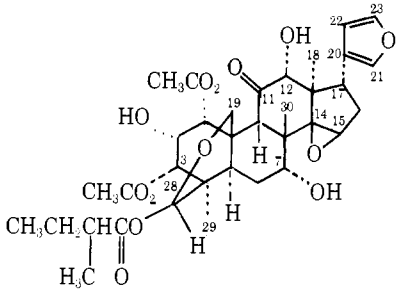
Isolation and Structure of Aphanastatin[1]

Sir:

Certain plants of the order Rutales, especially in the Simaroubaceae family, have a long history of use in primitive medicine for cancer treatment[2] and various amoebic, inflammatory, and malarial problems.[3] In recent years several very promising antineoplastic agents have been isolated from Simaroubaceae species.[3,4] As part of an initial study of the closely related Meliaceae family for potentially useful anticancer constituents we found extracts prepared from seeds of the Eastern Himalayan (India) plant *Aphanamixis grandifolia* Bl.[5] to markedly inhibit growth of the murine lymphocytic leukemia P388.[6] Now we are pleased to report that separation directed by bioassay (P388 cell line) of the *Aphanamixis g.* seed extract (aqueous) led to discovery of a new highly cytotoxic (P388 ED_{50} 0.065 μg/mL) limonoid designated aphanastatin (**1**).[7]



1

A chloroform-soluble fraction (P388 ED_{50} 0.33 μg/mL) of the water extract was subjected to successive gradient elution (chloroform–methanol) chromatographic separations on silica gel (E. Merck) to afford aphanastatin (**1**) as crystals (from chloroform–methanol) decomposing at 269–271 °C, $[\alpha]^{22}_D$ −38.9° (*c* 0.46, 1:24 pyridine–methanol), and $CD\Delta^{\epsilon}$ −2.88 (311 nm) in the same solvent, corresponding to molecular formula $C_{35}H_{46}O_{13}$ (mass spectrum *m/e* 674.2907 for M^+).

The mass spectrum of aphanastatin showed significant fragmentation ions at *m/e* 572.2252 ($C_{30}H_{36}O_{11}$), 512.2049 ($C_{28}H_{32}O_9$), and 452.1824 ($C_{26}H_{28}O_7$) corresponding to successive loss from the molecular ion of 1 mol of pentanoic acid and 2 mol of acetic acid. Interpretation of these data and that from the 250-MHz ^1H NMR spectrum[8] (methyl protons at δ 0.81 (s, 3 H), 0.83 (t, 3 H, J = 7.5 Hz), 1.03 (d, 3 H, J = 7.5 Hz), 1.10 (s, 3 H), 1.29 (s, 3 H), acetate methyls at 2.02 and 2.08, and other protons at 3.74 (s, 1 H, H-7), 3.74 (s, 1 H, H-15),[11] 4.10 (s, 1 H, H-9), 4.38 (s, 1 H, H-12), 4.46 (q, 1 H, J = 13.7 Hz, H-19), 4.89 (t, 1 H, J = 5 Hz, H-2), 5.58 (d, 1 H, J = 5 Hz, H-3, 5.82 (1 H, H-28), 5.96 (d, 1 H, J = 5 Hz, H-1), 6.62 (s, 1 H, H-22), 7.25 (s, 1 H, H-21), and 7.52 (s, 1 H, H-23)) suggested compound **1** to be an α-methyl butyrate diacetate derivative of a tetranortriterpene.[9] The ^1H NMR data also indicated the presence of a furan ring and double-resonance experiments suggested presence of the system -CH(OAc)CH(OH)CH(OAc)-.

The structure of aphanastatin (**1**) was completely established by single-crystal x-ray analysis. Orthorhombic crystals of space group $P2_12_12_1$, a = 19.234 (3) Å, b = 14.206 (3) Å, c = 12.363 (5) Å, Z = 4, d_{calcd} = 1.326, were employed. Single-crystal x-ray diffraction data were measured with a Philips PW 1100 diffractometer using the ω–2θ scan technique with graphite monochromated Cu Kα radiation. The structure was solved by direct methods.[10] Full-matrix least-square refinement, with anisotropic temperature factors for the nonhydrogen atoms, resulted in an R factor of 0.050, based on 2060 observed reflexions.

The positions and configuration of substituents are 1α-OAc, 2α-OH, 3α-OAc, 4α-CH_3, 5α-H, 7α-OH, 8β-CH_3, 9α-H, 11-oxo, 12α-OH, 13α-CH_3, 14β,15β-epoxy, and 17α-C_4H_3O (furan ring). Ring C has a twist boat conformation and ring D takes an envelope form with C-17 out of the mean plane through the other four atoms by 0.58 Å. The dihedral angles between H-7 and the two hydrogen atoms bonded to C-6 are +60 and −60° and those between H-15 and the two hydrogen atoms bonded to C-16 are +48° and −72°. The dihedral angle between H-22 and H-23 is −3°.

The quassinoids, limonoids, and meliacins are assumed to have the same biosynthetic precursor.[9] Since the triterpenoid biogenetic origin of the quassinoids has been experimentally

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