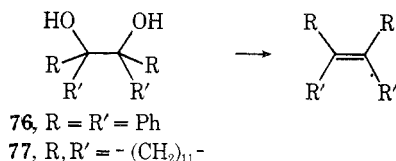


hydrobenzoin, is reduced to *trans*-stilbene by a $\text{TiCl}_3\text{-CH}_3\text{Li}$ reagent¹¹ [presumably *via* Ti(II)], and we have further demonstrated that treatment of either benzpinacol (76) or the dilithium salt of cyclododecanone pinacol (77) with the $\text{LiAlH}_4\text{-TiCl}_3$ reagent also yields the corresponding olefins. Thus, the reagent affords a method for the reduction of 1,2-diols to olefins and competes favorably with other methods of doing the transformation.²⁷



One further observation which should be made is that, if LiAlH_4 is serving merely to reduce Ti(III) to Ti(II), then other reagent systems producing Ti(II) might also effect the coupling reaction. There have in fact been two recent reports on the use of $\text{TiCl}_4\text{-Zn}$ ²⁸ and $\text{TiCl}_4\text{-Mg}$ ²⁹ reagents to couple aromatic ketones. Both reagents fail for aliphatic ketones, however. We ourselves have also found that a variety of reducing agents, including LiBH_4 , LiH , and CaH_2 , will reduce either TiCl_3 or TiCl_4 to a reagent which will couple aromatic ketones.

The coupling of aliphatic ketones is considerably more difficult, however, and in our experience only the $\text{LiAlH}_4\text{-TiCl}_3$ reagent has performed satisfactorily. The rate-determining step in the coupling must involve loss of oxygen from the pinacol (pinacol formation must be faster than subsequent deoxygena-

tion since pinacols can be isolated as intermediates). Certainly the deoxygenation should be easier in aromatic cases than in aliphatic cases since the C-O bond involved is benzylic. We have no explanation for the enhanced reactivity of the $\text{LiAlH}_4\text{-TiCl}_3$ system, but studies are in progress to further elucidate the matter.

Conclusion

The organic chemistry of low-valent titanium has undergone a renaissance in the past decade, but, as indicated at several places in the text, much work remains yet to be done. A study of the reduction of other species with S-O bonds is not complete, and the reductive elimination of vicinal dihalides and alkoxy halides needs more examination. Most exciting at the moment, however, is the continuing study of $\text{LiAlH}_4\text{-TiCl}_3$, and many questions remain to be answered: Can the reagent be used to form rings from 1,5- and 1,6-diketones (a "reverse ozonolysis")? Is the diol to olefin reduction stereospecific? Do epoxides reduce to olefins, and, if so, is the reaction stereospecific? Do other functional groups such as alkyl halides and acyloins reduce? Do allylic and benzylic alcohols couple to symmetrical hydrocarbons with the reagent? Low-valency titanium reagents undoubtedly hold many new surprises for the organic chemist, and with the wide range of reactions already discovered, it seems quite doubtful that titanium chemistry will sink into obscurity again.

I am fortunate to have had the assistance of three able and energetic graduate students, Mr. Jack Melton, Dr. Larry Blaszcak, and Mr. Michael Fleming, on parts of this work. Partial support was provided by a fellowship grant from the Alfred P. Sloan Foundation and by a research grant from the National Science Foundation (GP 28173).

(27) See K. B. Sharpless and T. C. Flood, *J. Chem. Soc., Chem. Commun.*, 370 (1972), and references therein.

(28) T. Mukaiyama, T. Sato, and J. Hanna, *Chem. Lett.*, 1041 (1973).

(29) S. Tyrlik and I. Wolochowicz, *Bull. Soc. Chim. Fr.*, 2147 (1973).

Propellanes as Stereochemical Models

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"The world is chiral and clinal; enjoy symmetry wherever you find it." Although V. Prelog offered this advice to my daughter, I too have followed it. The result is esthetically pleasing and chemically exciting. Without doubt propellanes are fine models for stereochemical studies in which symmetry is a cardi-

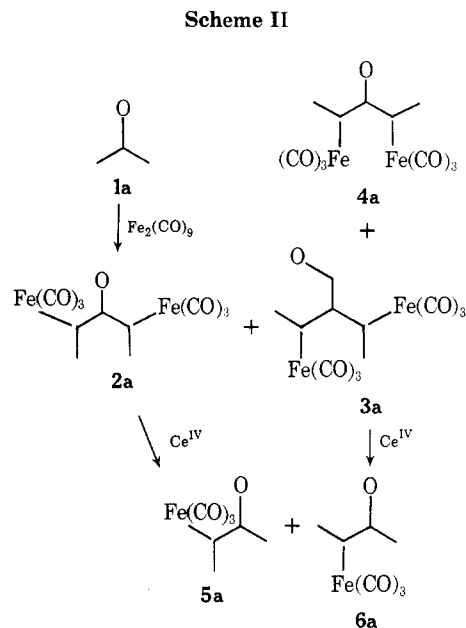
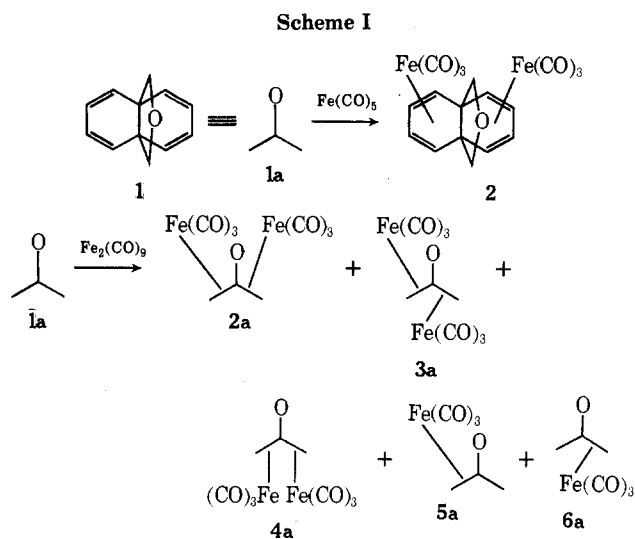
nal component. The following Account constitutes an attempt to prove this thesis.

When the tetraenic propellane ether **1** was treated with iron pentacarbonyl, a single product, **2**, was obtained in high yield.¹ But we were equally pleased when we obtained five distinct products upon treatment of **1** with $\text{Fe}_2(\text{CO})_9$. These were separated by column chromatography, and it turned out that this time **2** was accompanied by two isomeric bis- $\text{Fe}(\text{CO})_3$ derivatives and two mono- $\text{Fe}(\text{CO})_3$ derivatives.

From the viewpoint of symmetry this is perhaps

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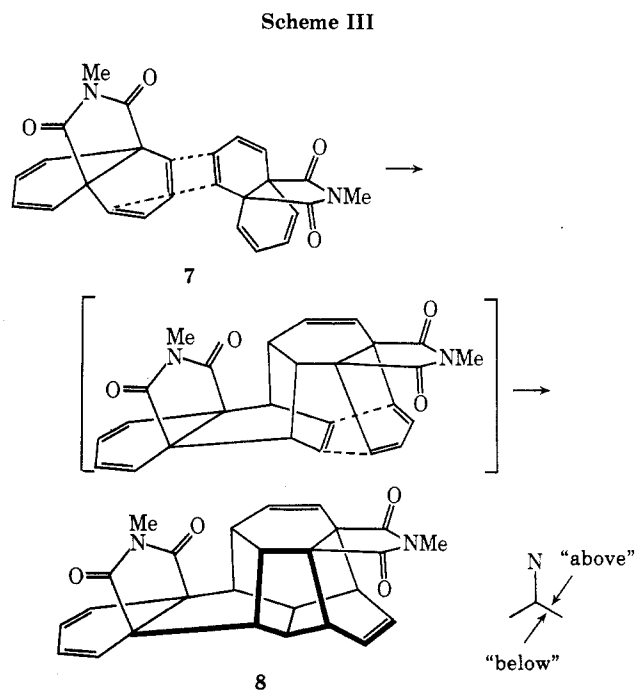
(1) J. Altman, E. Cohen, T. Maymon, J. B. Petersen, N. Reshef, and D. Ginsburg, *Tetrahedron*, **25**, 5115 (1969).



best observed by using formulas of the "a" series which represent the profile of the molecule as one observes it looking down the axis of the conjoining bond (Scheme I).

The question now is which bis complex is which and which mono complex is which. The answer has been partly anticipated in Scheme I, as the structure written for **2a** was justified only after we had iron-clad proof through an X-ray diffraction study.² The structure of **3** was clear on the basis of its nmr spectrum as the CH_2O protons exhibited an AB quartet while those of its isomeric bis complex **2** and **4** appeared as a four-proton singlet. Treatment of **2** with the equivalent amount of ceric ammonium nitrate gave **5** while **3** gave **6** with ceric ion. Once the structure of **2** was unequivocally established, the structures of all of the other compounds in Scheme I fell into place.^{2a} It is necessary, however, on the basis of knowledge gleaned from the X-ray studies of **2** and of **3**, to specify more accurately the shape of the silhouettes given in Scheme I. The cyclohexadiene rings in **2** and **3** appear as boat conformations. For this reason we assume these to obtain also in **4-6** although these structures were not established by X-ray diffraction. There is no reason to change the silhouette of **1** in which the cyclohexadiene ring must be planar. The planarity of the ether ring in **2^b** is probably the result of averaging of the two possible enantiomeric envelope conformations, but the very interesting result obtained for **3** where one envelope is stable has been explained in electronic terms.³ As the corresponding $\text{Fe}(\text{CO})_3$ group withdraws electrons from the appropriate cyclohexadiene ring (the left ring as shown in Scheme II) the ether ring envelope leans toward this ring and the distance between the oxygen and the cyclohexadiene ring permits the inference that, by so leaning, it replenishes the charge depleted from this ring. We are not being picayune in rewriting Scheme I more accurately in the form of Scheme II. We shall see that molecular conformation in this series of compounds permits explanation of the steric course of reactions to be discussed below.

We shall see below how the above work later tied in with another study of the steric course of completely different reactions of the same substrate (Schemes IV-VII). This stemmed from a study of thermal electrocyclic reactions of tetraenic propellanes. We found first that heating of the tetraenic methylimide **7** afforded a dimer, **8**. Elucidation of the structure by indor spectroscopy and by application of the nuclear Overhauser effect showed⁴ that it is possible to interpret the steric course of the reaction as a simple Diels-Alder cycloaddition between 2 mol of **7** one of which acts as a diene, the other as the dienophilic component, followed by a second, this time *intramolecular* step, also of the Diels-Alder type (Scheme III). The dienophile attacks the diene from above, not from below, as defined in the arbitrary formulation in Scheme III.



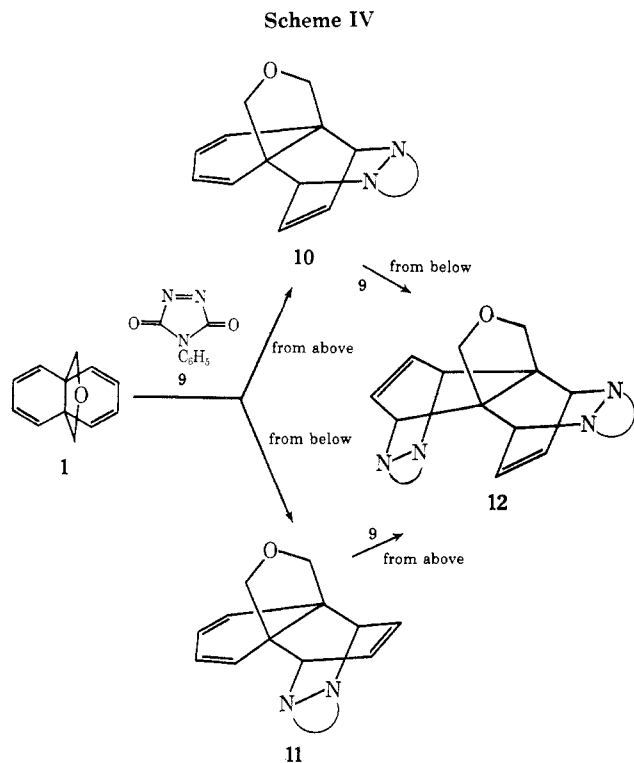
(2) (a) K. B. Birnbaum, J. Altman, T. Maymon, and D. Ginsburg, *Tetrahedron Lett.*, 2051 (1970); (b) K. B. Birnbaum, *Acta Crystallogr., Sect. B*, **28**, 161 (1972).

(3) G. I. Birnbaum, *J. Amer. Chem. Soc.*, **94**, 2455 (1972).

(4) O. Sciacovelli, W. von Philipsborn, C. Amith, and D. Ginsburg, *Tetrahedron*, **26**, 4589 (1970).

It was of interest to study the steric course of the Diels-Alder reaction of our tetraenic substrates with dienophiles of simpler structure than, say, **7** which accommodately performed both as diene and as dienophile. There did not appear to be an *a priori* reason why **1** or **7** should not give both mono and bis adducts but, in the event, it soon became clear that though **7** afforded both, **1** gave only mono adducts and we conjectured that this is due to relatively higher steric hindrance in **1** as compared to **7**, the difference between the two being CH₂ groups in **1** vs. CO groups in **7**, α to the respective heteroatoms.⁵ We soon found, however, that, given a very reactive dienophile such as 4-phenyl-1,2,4-triazoline-3,5-dione (**9**) a second mole of dienophile can be induced to react even with mono adducts of **1**.

The dienophile gives with **1** the unsymmetrical bis adduct **12** which is completely analogous from the viewpoint of symmetry to the bis-Fe(CO)₃ complex **3**. Here, too, the CH₂O protons exhibited an AB quartet in the nmr spectrum. This, of course, tells us nothing about the chronology of attack by the dienophile since attack from above by the first mole of dienophile followed by attack from below of the mono adduct would give the same product as the reverse chronology of events (Scheme IV). How can one prevent attack, for example from above? The simplest route to prophetic insight is that of hindsight. But since we did not have the benefit of hindsight we had to do it the hard way and conceive a suitable idea. This idea may even have been a nice one while it lasted.

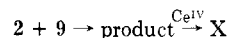


We had available the bis complex **2** in good yield, if Fe(CO)₅ was used to prepare it. Both top faces were blocked by Fe(CO)₃ groups. Thus, if our very reactive dienophile were sufficiently reactive to

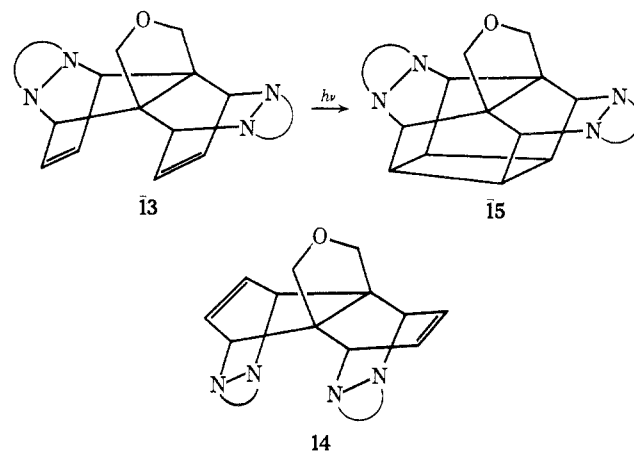
displace an Fe(CO)₃ group by backside attack (*i.e.*, from below), and if we could displace the Fe(CO)₃ groups stepwise, then we would be able to correlate our products with those obtained from uncomplexed **1** and thus interpret the chronology of the attack leading to **12**.

When **2** was treated with a large excess of **9** in acetone, eventually, after hours of heating *vis-à-vis* seconds required for reaction of **1** with **9**, a mono(iron tricarbonyl) derivative of a mono-Diels-Alder adduct was obtained. One mole of dienophile indeed displaced one of the two Fe(CO)₃ groups. The remaining Fe(CO)₃ group was removed by ceric ion. The product was an isomer of that obtained from **1** and **1** mol of **9**. Thus, if $1 + 9 \rightarrow 10$, then $2 + 9 \rightarrow 11$ and inversion of configuration indeed took place in the latter reaction. But, if one considers the possibility that when a large excess of **9** is present it is possible that **1** mol of **9** displaces CO from iron and if the complex formed is unstable and decomposes, then the free cyclohexadiene ring may react with another mole of **9** attacking from the same side which had been complexed to Fe(CO)₃, *i.e.*, displacement may have occurred with retention of configuration. Reasoning backwards, then, it may be that $2 + 9 \rightarrow 10$ and, if so, then the product of reaction of $1 + 9$ must have been **11**.

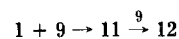
Now, when the product X, whether it be **10** or **11** formed in the sequence



was treated with an additional mole of **9**, a bis adduct was obtained. This exhibited a singlet for the CH₂O protons and was an isomer of **12**. Such a symmetrical bis adduct must be either **13** or **14**. The for-

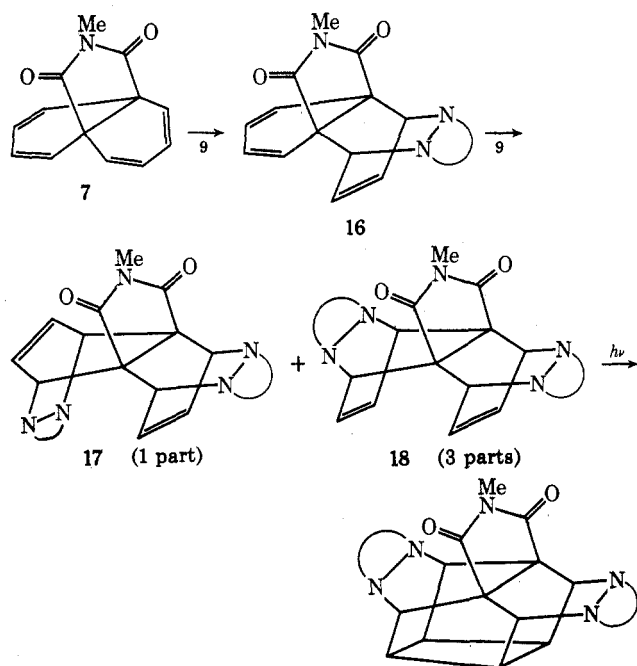


mer is formed by retention of the configuration of **2**, the latter by inversion. The choice between the two was made in an unequivocal way. Irradiation caused four vinylic protons to disappear and four cyclobutyl protons to appear in the nmr spectrum of the product **15**. Hence the symmetrical bis adduct is **13**. Since both the first and second mole of dienophile had to attack from above to give **13**, the monoadduct **X** must needs have been **10**. Since the only isomer of **10** is **11**, then the product of $1 + 9$ must be **11** and the steric course of reaction leading to **12** must have been, chronologically



(5) M. Korat, D. Tatarsky, and D. Ginsburg, *Tetrahedron*, **28**, 2315 (1972).

Scheme V



The first mole of dienophile attacks the ether **1** from below, the second from above.

When the tetraenic methylimide **7** was treated with 1 mol of **9**, a mono adduct, **16**, was isolated in 93% yield. The second mole of dienophile afforded two bis adducts in the ratio 3:1.^{5,6} Irradiation of the major product **18** again laid the floor of the house (Scheme V).

Thus, the first mole of the same dienophile **9** attacks the methylimide from the top face (as in the case of dimerization of **7**), in contrast to the ether **1** which is attacked from the bottom face. In both substrates the second mole of **9** attacks the top face. Why?

We have explained the attack of **1** from below on the basis of steric hindrance exerted by the CH_2O hydrogen atoms to attack from above. These hydrogens do not exist in the methylimide **7** which is attacked from above. Still, the molecular shape of **7** is not all that different from that of **1**. Why is not **7** attacked from below, at least in part? We explain this by invoking second-order orbital effects. The transition state for attack from below has nothing to stabilize it except the potential 1,4 interaction with the conjugated diene system, but this is the first-order effect. Such stabilization exists also in the transition state from above except that here there is extra second-order stabilization by overlap between the nitrogen lone pair orbitals of the dienophile double bond and the optimally situated orbitals of the carbonyl groups. Since the Diels-Alder reaction permits establishment of an equilibrium, the thermodynamically more stable isomer may be obtained *exclusively* and **16** is therefore formed *via* the most stable transition state.

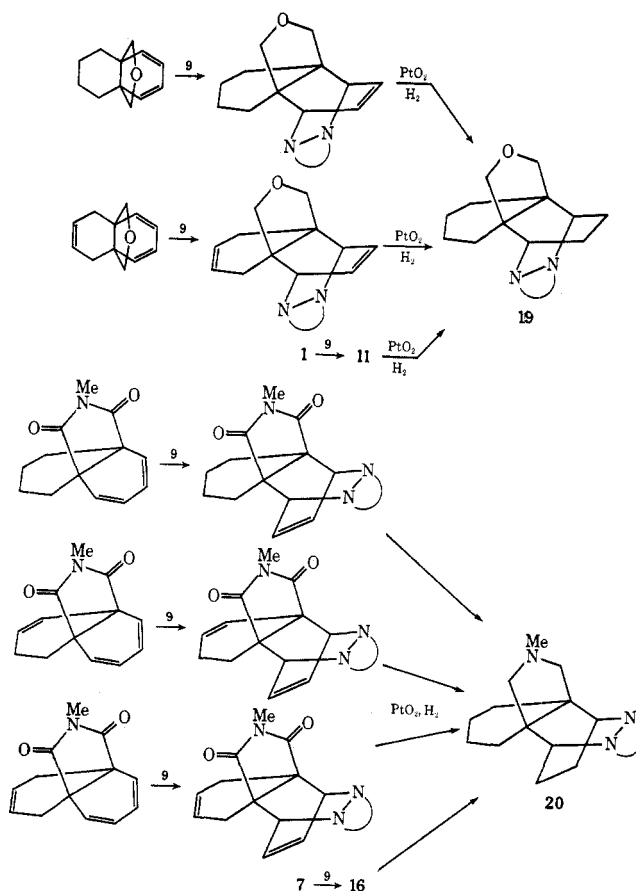
So far, this interpretation has been tested for dienes and trienes related to **1** and to **7**. Despite the different shape of the cyclohexane or cyclohexene ring present in these compounds and the different

steric effect exerted by such ring upon the pertinent transition state, all of the [4.4.3]propellane ethers were attacked from below and all of the methylimides were attacked from above.⁷ In the former cases where the only additional electronic stabilization may come from ether-oxygen lone pairs and these are not spatially disposed in the optimal manner for overlap with the $\text{N}=\text{N}$ double bond or nitrogen lone pairs of the dienophile, this is ineffectual and the steric hindrance exerted by the CH_2O hydrogens predominates. In the latter cases, this steric factor is absent and the change from a relatively planar third (cyclohexadiene) ring to a chair (in a third cyclohexane ring) or to a half-chair (in a third cyclohexene ring)⁸ is not enough to affect the steric course of attack. The electronic stabilization of the transition state for top-side attack predominates.

Scheme VI illustrates how the above results were correlated with those in Schemes IV and V. Since **19** and **20** are the common perhydro products obtained from all of the ethers and all of the methylimides, respectively, and the structures of **11** and **16** were unequivocally established earlier, the structures and configurations of all of the compounds in Scheme VI follow.

Thus far, we have only discussed the formation of mono adducts. Why is it that the second equivalent of dienophile reacts with the monoadduct, whether it be **10** or **11**, from above, despite the fact that there

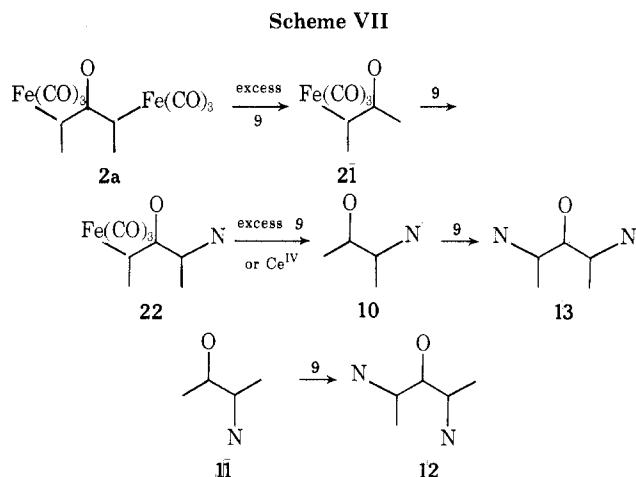
Scheme VI



(7) C. Amith and D. Ginsburg, to be published.

(8) This is assumed by analogy to the respective conformations of these rings in [4.4.4]propellane and [4.4.4]propella-3,8,12-triene. Cf. O. Ermer, R. Gerdil, and J. D. Dunitz, *Helv. Chim. Acta*, 54, 2476 (1971).

are still two hydrogen atoms of the CH_2O type present? We claimed that their enantiotopic neighbors in **1** prevented approach of the first equivalent of dienophile from above. Why should this not hold true also for the second equivalent? And why, for that matter, is $\text{Fe}(\text{CO})_3$ in **2** replaced by the dienophile with retention and not by inversion of configuration? The silhouettes in Scheme VII provide the answers.



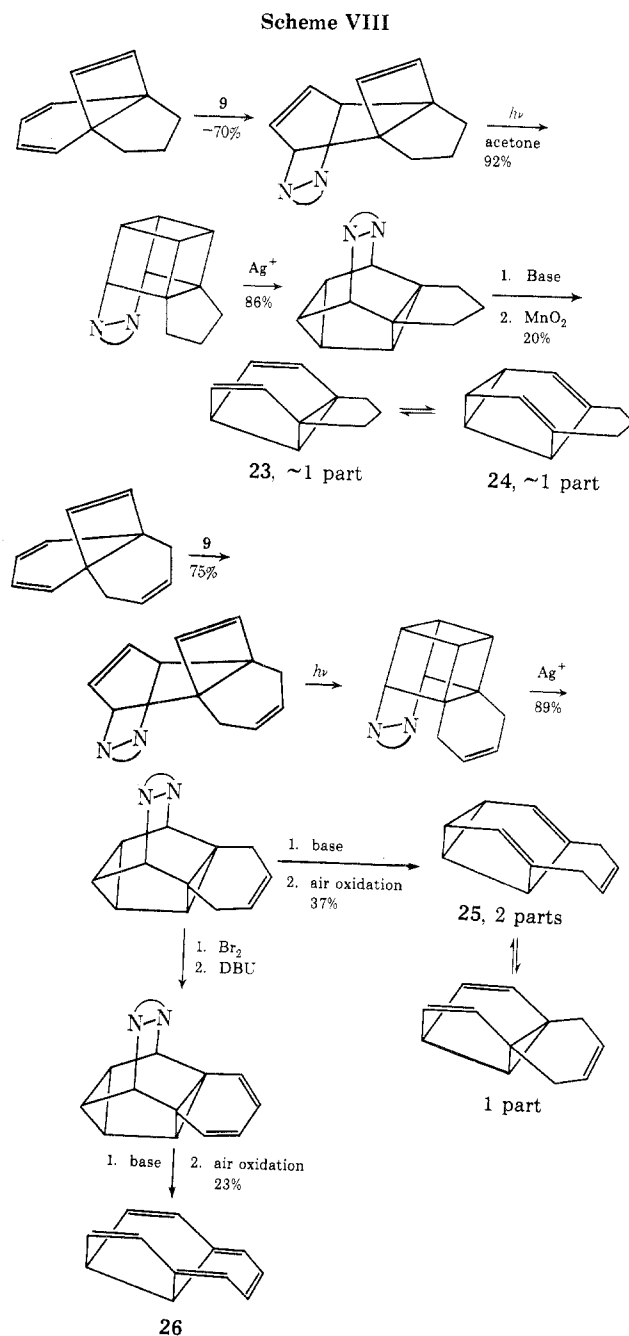
The explanation is so simple as to appear almost trivial. Once a boatlike structure exists in any of these compounds, it exerts much more steric hindrance to attack from below than do two hydrogen atoms from above. Thus the reaction course chosen is the lesser of two evils. The necessarily covalent boat portion of the diazabicyclo[2.2.2]octane system in either **10** or **11** thus forces **9** to attack from above.

When **2a** is treated with an excess of **9** and the first $\text{Fe}(\text{CO})_3$ group is removed, we still have in **21** the adjacent cyclohexadiene complexed to $\text{Fe}(\text{CO})_3$ in a boatlike conformation. Hence **9** reacts from above, forming a product, **22**, which this time has at its bottom two boatlike conformations, one in the diazabicyclo[2.2.2]octane, the other due to the metallic complex. When excess **9** or ceric ion removes this $\text{Fe}(\text{CO})_3$ group, **10** is obtained and this, of course, gives **13**.

The problem of the configuration of various propellane Diels-Alder adducts has been studied by others. Although various authors have conducted Diels-Alder reactions with suitable propelladienes, the proposed structures were not always established with certainty. There is a notable case of such reactions where this complaint should not be made.⁹ On the contrary, a photochemical reaction was again used to establish unequivocally the configurations of the Diels-Alder adducts which were intermediates in an elegant study of fluxional isomerism in 2,8-bridged semibullvalene derivatives.

Scheme VIII summarizes the transformations involved.

This reaction scheme includes, besides the photochemical steps which prove that the dienophile has attacked each of the cyclohexadiene rings from below, a rearrangement step employing Ag^+ . When the final products are reached in each sequence, it



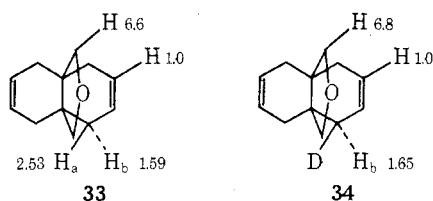
turns out that the one obtained from the [4.3.2]propellane precursor consists of nearly equal proportions of the propellane form **23** and its open fluxional isomer **24**. In the [4.4.2] case the equilibrium in the product mixture is in favor of the open form **25** which predominates by 2:1. In the same series, introduction of the extra double bond causes stabilization of the open form **26** in which there is some evidence in the nmr spectrum for diamagnetic ring current. But for reasons given by the authors they prefer to investigate the system further before deciding whether the pentaene structure should be better represented in a delocalized manner involving three or possibly five of the double bonds.

The Diels-Alder bis adducts of known configuration **12** and **13** were used as substrates in order to prepare bisazo propellanes which could then be subjected to thermolysis and photolysis.¹⁰ We used

(9) L. A. Paquette, R. E. Wingard, Jr., and R. K. Russell, *J. Amer. Chem. Soc.*, **94**, 4739 (1972).

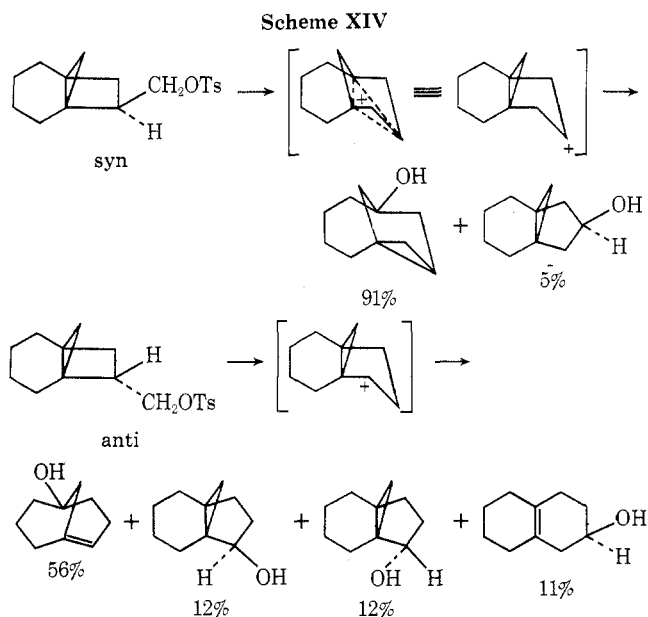
(10) M. Korat and D. Ginsburg, *Tetrahedron*, **29**, 2373 (1973).

ance.¹⁴ However, we have carried out a study in which it has been possible to use $\text{Eu}(\text{DPM})_3$ in order to determine the steric course of hydrogenation of the tetraenic ether **1** using phenanthrene- $\text{Cr}(\text{CO})_3$ as the homogeneous catalyst.¹⁵ Although, in principle, the 1,4 reduction usually brought about by such catalysts may occur from the top of each cyclohexadiene face, from the bottom of each, or from the top of one and the bottom of the other, it was found using the shift reagent that deuterium, and therefore hydrogen, is delivered from the top of each face. No matter which conformation is chosen by the cyclohexene ring after hydrogenation, the allylic protons marked H_a are closer to the ether-oxygen atom in **33** than those marked H_b . Observation of H_a and H_b at different concentrations of shift reagent in the undeuterated **33** and in its deuterated analog allowed plotting $\delta\Delta\nu$ vs. concentrations of $[\text{Eu}(\text{DPM})_3]/[\text{diene}]$. The relative slopes of the straight lines obtained in this way are recorded in formulas **33** and **34** for the



appropriate protons. From these figures it may be unequivocally deduced that reduction of each ring occurs from the top side, perhaps because of some precoordination of the ether-oxygen atom with the hydrogenation catalyst. A similar initial coordination may be invoked to explain the exclusive formation of **2** when **1** is treated with iron pentacarbonyl (Scheme I). (It is not surprising that $\text{Fe}_2(\text{CO})_9$ gives a multitude of products because $\text{Fe}(\text{CO})_4$ rather than $\text{Fe}(\text{CO})_5$ is presumed to be the reactive species in analogy to other known cases.)

Gassman has recently shown the great selectivity during the course of solvolysis of epimeric tosyloxy-

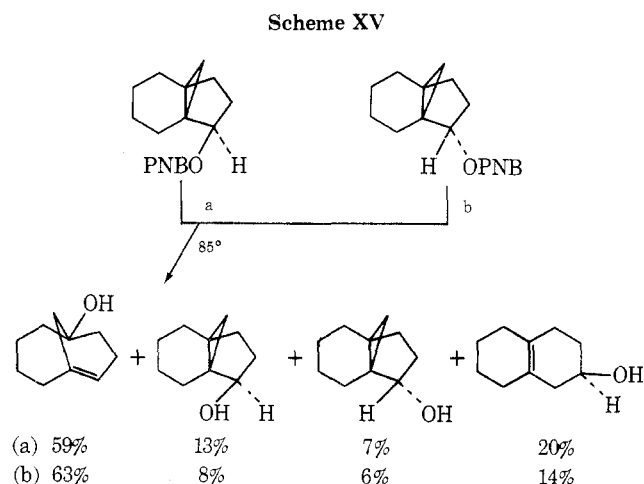


(14) C. Amith and D. Ginsburg, unpublished results.

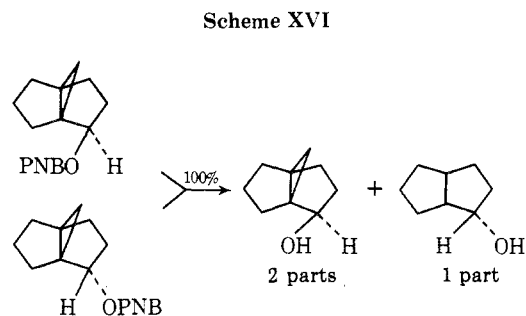
(15) C. Amith, M. Cais, D. Fraenkel, and D. Ginsburg, *Heterocycles*, **1**, 39 (1973).

methyl derivatives belonging to the [4.2.1]propellane series. Although the isomers undergo similar solvolysis in aqueous acetone insofar as rate is concerned, product studies have shown that they rearrange selectively *via* two entirely different cations (Scheme XIV).¹⁶

This should be compared with the results in Scheme XV where epimeric *p*-nitrobenzoates of the [4.3.1]propellane series were subjected to solvolysis under similar conditions.¹⁷ Clearly, these proceed *via* the same cation as postulated for the anti tosylate in Scheme XIV. The same products are obtained, albeit not exactly in the same proportions. At 10% reaction the respective ratios from path a were 70:25:4:1 and from path b 68:30:1:trace, indicating that the last two products are resultants of the first two, primary, products. Also indicated is the fact that in this case the product ratios from either epimer are essentially the same, pointing to an identical cationic intermediate.



There is a common cationic intermediate also during solvolysis of *p*-nitrobenzoates in the [3.3.1]propellane series. Both esters of alcohols shown in Scheme XIV give a 2:1 mixture of products upon solvolysis in aqueous acetone at 100° (Scheme XVI).



Quo vadimus in this stereochemical chapter of propellane research?

We are continuing to explore the effectiveness of lanthanide shift reagents in assigning structure and conformation to various propellanes. The experimental problems involved, *e.g.*, precipitation from solution of a complex of one isomer *vs.* an isomeric com-

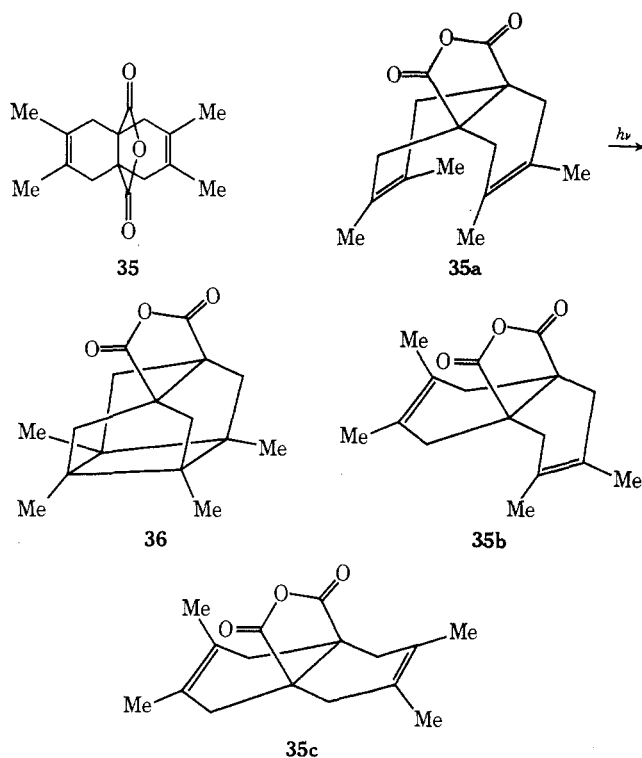
(16) P. G. Gassman and E. A. Armour, *J. Amer. Chem. Soc.*, **95**, 6129 (1973).

(17) P. G. Gassman, R. N. Steppel, and E. A. Armour, *Tetrahedron Lett.*, 3287 (1973).

plex which remains in solution, often prevent this tool from being used to maximum avail.

We are probing whether various propellanes exist in uniquely stable conformations or whether certain reactions occur as they do because the reacting conformation is removed from a conformational equilibrium mixture in the course of these reactions. It is not possible, for example, to state without further investigation whether the photochemical intramolecular [2 + 2] cycloaddition shown in Scheme XVII is due to the fact that **35** exists in solution uniquely as the stable conformation **35a** or whether there is a conformational equilibrium comprising, *inter alia*, **35a**, **35b**, and **35c**, but since the flip-flop of the rings involved is slower than excitation, the excited state, when it finds itself in a conformation approximating **35a**, reacts to form **36**.¹⁸ It is by no means implicit in Scheme XVII that only boat forms are proper for the cyclohexene rings (*cf.* ref 8).

Scheme XVII



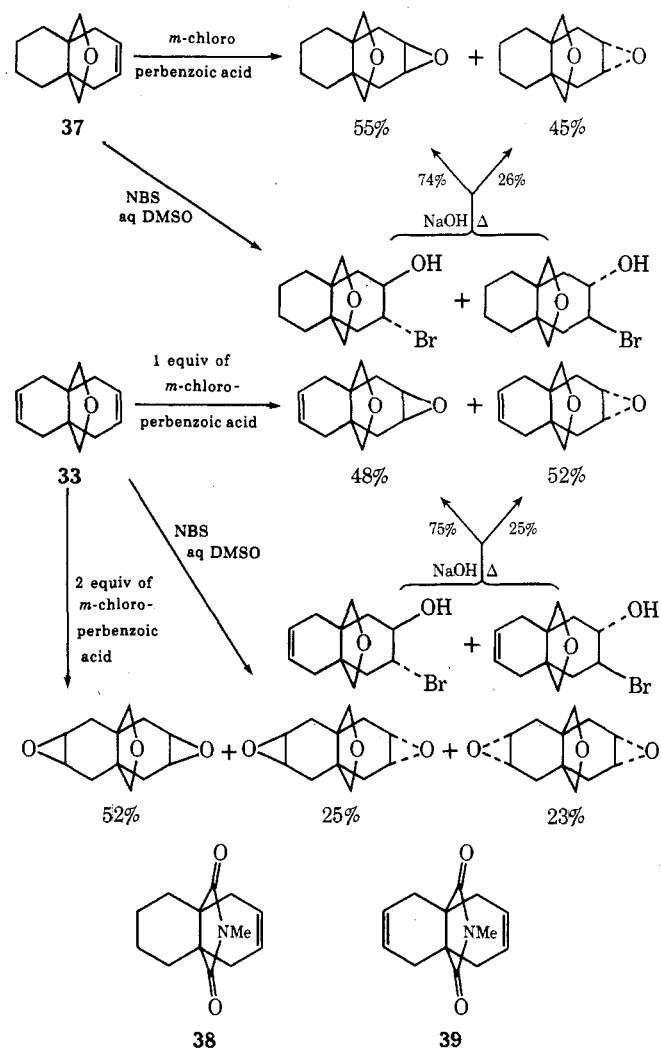
We are employing as models compounds such as the monoolefins **37** and **38** and the dienes **33** and **39**. Their molecular shape need not be, nor is it, exactly similar to that of the corresponding tetraenes **1** and **7**.

Reactions of these substrates with electrophilic reagents are apt to permit conclusions to be drawn regarding both structure of substrate and steric course of reaction. In the diene cases it may also be possible to employ the two alicyclic rings as trapezes for acrobatic groups (*cf.* Scheme XII¹²).

(18) W. B. Avila and R. A. Silva, *Chem. Commun.*, 94 (1970).

We exemplify by some simple reactions which are summarized in Scheme XVIII.¹⁹

Scheme XVIII



These results are tentative as there is no real proof that syn epoxides are indeed syn and that their configuration should not be reversed to anti. The only certain structure is that of the unsymmetrical bis epoxide which again exhibits an AB quartet for its CH₂O protons *vs.* singlets for the other two isomers isolated. Since the lanthanide-shifted spectra did not give clear-cut results and since a 50:50 chance of being configurationally correct is neither satisfactory nor satisfying, it is clear that one needs to break the vicious circle by effecting transannular reactions which would fit all of the mosaic chips in place. Thus, in answer to the question "*quo vadimus?*" this is one of the directions whither we go.

It has been a pleasure to be associated with Messrs. (now Drs.) C. Amith and M. Korat, and with D. Tatarsky who earned an M.Sc. degree through the vehicle of propellanes. Mr. W. J. W. Mayer is at present working on his Doctoral thesis and thanks the DAAD for a stipend which makes this possible. We owe much to stimulation from colleagues working in the field. Their names are cited in the references.

(19) W. J. W. Mayer and D. Ginsburg, unpublished results.