for an additional source of unpaired spin density at the heme periphery, namely the cation radical. Current studies in our laboratory on isotope labeling of the heme are expected to provide a more definitive characterization of the second oxidizing equivalent in HRP-I.

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Gerd N. La Mar,* Jeffrey S. de Ropp
Department of Chemistry, University of California
Davis, California 95616
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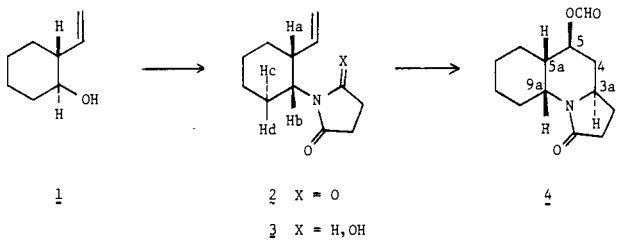
Effect of A$^{(1,3)}$ Strain on the Stereochemical Course of *N*-Acyliminium Ion Cyclizations

Sir:

N-Acyliminium ion initiated olefin cyclizations have been documented as a potent tool in alkaloid synthesis.[1] Although a number of stereochemical features of these reactions have been delineated,[2] the effect of asymmetric centers on their stereochemical course has received little attention.[3] Herein are reported results encountered during the course of studies directed toward a synthesis of the *Dendrobatid* alkaloid gephyrotoxin (Scheme I)[4] which illustrate that chiral centers can exert profound influence over the stereochemistry of such cyclizations.

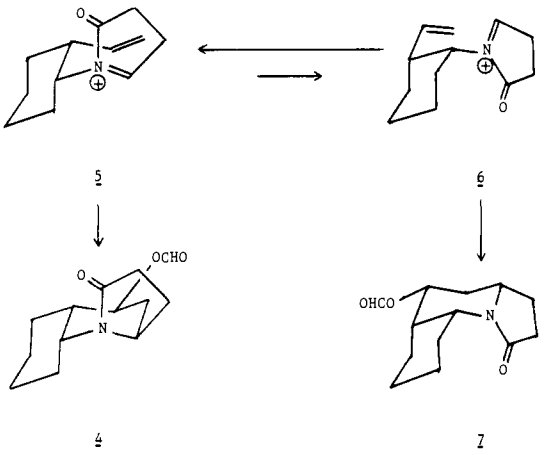
Treatment of *trans*-2-vinylcyclohexanol (**1**)[5] with diethyl azodicarboxylate in the presence of triphenylphosphine and succinimide[6] gave imide **2** (mp 63–66 °C; 50%). Reduction of **2** with diisobutylaluminum hydride[7] afforded carbinolamide

Scheme I



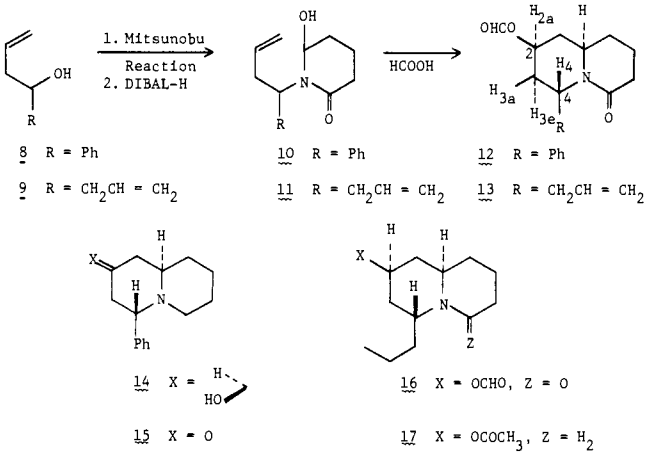
1 **2** X = O; **3** X = H,OH **4**

Scheme II



4 **5** **6** **7**

Scheme III



8 R = Ph; **9** R = $CH_2CH=CH_2$ **10** R = Ph; **11** R = $CH_2CH=CH_2$ **12** R = Ph; **13** R = $CH_2CH=CH_2$

14 X = H, HO; **15** X = O **16** X = OCHO, Z = O; **17** X = $OCOCH_3$, Z = H_2

3 as a mixture of diastereomers (mp 93–108 °C; 57%). Treatment of **3** with formic acid (25 °C; 30 min) gave an 85% yield of tricyclic lactam **4** (mp 100–102 °C). The stereochemical assignment for **4** followed from the coupling pattern of the C-5 proton, which appeared as a triplet of doublets (J = 11, 11, 4 Hz) at δ 5.36 ($CDCl_3$).[8] Of the four possible *cis*-decahydroquinolines which could have resulted from the *N*-acyliminium ion cyclization, only **4** can adopt a conformation in which the C-5 proton affords two anti and one gauche coupling to protons at C-4 and C-5a.[9]

Two factors may be responsible for the stereoselective conversion of **3** into **4.** The cyclization of **3** most likely proceeds through an *N*-acyliminium ion which can adopt chair-chair conformations **5** and **6** (Scheme II). ^{1}H NMR analysis indicates that imide **2** adopts a chair conformation in which the vinyl group occupies an axial site (J_{ab} = 4, J_{bc} = 12, J_{bd} = 4 Hz). This suggests that **5** represents the most stable conformation of the *N*-acyliminium ion. In addition to the ground-state energy difference between the conformations leading to **4** and its C-3a,5 isomer **7**, it is probable that the E_{act} for conversion of **6** into **7** is greater than that for conversion of **5** into

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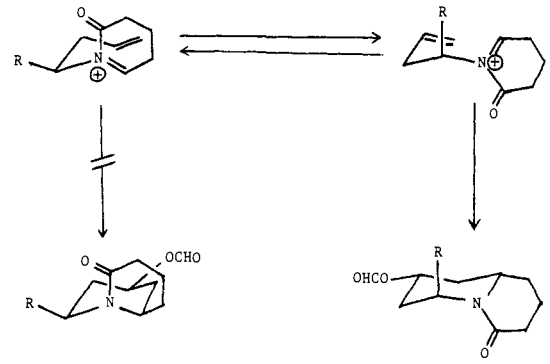
Scheme IV



4 owing to the development of a severe $A^{(1,3)}$ interaction in **7**.[10,11]

To evaluate the effect of $A^{(1,3)}$ strain on the stereochemical course of *N*-acyliminium ion cyclizations in a conformationally nonbiased system, carbinolamides **10** and **11** were prepared as outlined in Scheme III.[12] Treatment of **10** and **11** with formic acid (25 °C, 8-10 min) gave quinolizidinones **12** (mp 135-137 °C) and **13** (mp 72-74 °C) in 63 and 71% yields, respectively. Only small amounts (2-5%) of substances stereoisomeric to **12** and **13** were formed in these cyclizations. The stereochemistry of **12** was established by conversion into quinolizidine **14**[13] ($LiAlH_4$, mp 97-99 °C; 72%) and subsequent oxidation to known quinolizidinone **15**[14] (Jones reagent, 70%). The stereochemical assignment for **13** was based on spectral data gathered on the dihydro derivative **16** (H_2, Pd/C; mp 73-75 °C; 95%), aminoacetate **17**, and **13** itself.[15] These results suggest that the *N*-acyliminium ions derived from **10** and **11** cyclize via chair conformations in which the incipient C-4 substituent occupies an axial site (Scheme IV), in contrast to the equatorial orientation of substituents usually observed in olefin cyclizations and other reactions whose transition-state geometries resemble chair cyclohexane.[17-19] This unusual observation can be attributed to the unfavorable development of $A^{(1,3)}$ strain in the transition states leading to C-4 isomers of **12** and **13**.

The results presented here indicate that $A^{(1,3)}$ strain is an important consideration in predicting the stereochemical course of certain *N*-acyliminium ion cyclizations. This and other applications of the $A^{(1,3)}$ strain concept to stereochemical problems in alkaloid synthesis are being explored in these laboratories.[20]

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David J. Hart

Department of Chemistry, The Ohio State University
Columbus, Ohio 43210

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Stabilities of Carbonium Ions in Solution. 10. A Thermochemical Comparison of the Relative Stabilities of Long-Lived 2-Norbornyl and Butyl Cations in SO_2ClF/SbF_5

Sir:

We report here a calorimetric determination of the heats of isomerization of the secondary 4-methyl-2-norbornyl cation to the tertiary 2-methyl-2-norbornyl ion in SO_2ClF/SbF_5 at low temperatures using methods described previously.[1-3] When compared with the corresponding heat of isomerism of the *sec*-butyl to the *tert*-butyl cation under the same conditions, we find that the rearrangement of the norbornyl system is considerably less exothermic than is that of the acyclic system. We believe that this is the most compelling piece of evidence yet presented in support of the notion that the 2-norbornyl ion enjoys special thermodynamic stability relative to other simple secondary carbonium ions. This in turn confers added significance on the question of the ion's structure—i.e., whether or not it is bridged—for, if, as has been argued,[4] the norbornyl ion has no special degree of stability relative to appropriate models, there is little reason to propose a special structural feature for it.

The reason why the present experiment is particularly illuminating regarding the relative stabilities of the isomeric secondary and tertiary ions is that *no neutral precursor molecules or radicals are involved in the comparison.* We have emphasized recently[3] that initial state contributions render equivocal all interpretations of ionic stabilities in terms of heats of ionization or rates of solvolysis. Very large (e.g., 10 kcal/mol) initial state contributions can confuse comparisons of secondary vs. tertiary halides for such processes.[5] Initial state contributions to the methylnorbornyl systems have also been discussed,[6] and strain in 2-methyl-2-*exo*-norbornyl chloride has been shown to contribute ~2 kcal/mol to its heat of ionization.

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