intermediates unaddressed.[11] Few experimental examples for the existence of such tetrahedral intermediates have appeared.[12,13]

In a pulsed, Fourier transform, ion cyclotron resonance spectrometer,[14] methyl chloroformate gives CO_2Cl^- and $Cl_2CO_2CH_3^-$ which act as primary chloride ion donors through reactions[15] 2-6.

$$ClCO_2CH_3 + e^- \rightarrow Cl^- + CH_3CO_2^\bullet \quad (2)$$

$$Cl^- + ClCO_2CH_3 \rightarrow CO_2Cl^- + CH_3Cl \quad (3)$$

$$CO_2Cl^- + ClCO_2CH_3 \rightarrow Cl_2CO_2CH_3^- + CO_2 \quad (4)$$

$$CO_2Cl^- + M \rightarrow MCl^- + CO_2 \quad (5)$$

$$Cl_2CO_2CH_3^- + M \rightarrow MCl^- + ClCO_2CH_3 \qquad M = CH_3OH,\ CF_3COCl \quad (6)$$

$$CH_3OH{\cdot}Cl^- + CF_3COCl \rightleftharpoons CF_3COCl{\cdot}Cl^- + CH_3OH \quad (7)$$

Complex ions $CH_3OH{\cdot}Cl^-$ and $CF_3COCl{\cdot}Cl^-$ are thus formed as a result of (5) and (6) when M = CH_3OH and CF_3COCl (Figure 1a). At 500 ms after the electron beam pulse, double-resonance ejection of all ions but $CH_3OH{\cdot}^{35}Cl^-$ (m/z 67) leaves only this single complex ion (Figure 1b). $CH_3OH{\cdot}^{35}Cl^-$ then transfers its chloride ion to neutral molecules present in the gas mixture. After an additional time delay (300 ms) long enough for reaction 7 to reach equilibrium, a mass spectrum is recorded (Figure 1c), and the peaks correspond to $CH_3OH{\cdot}^{35}Cl^-$ (m/z 67), $CF_3CO^{35}Cl{\cdot}^{35}Cl^-$ (m/z 167), and $CF_3CO^{37}Cl{\cdot}^{35}Cl^-$ (m/z 169). Equilibrium 7 was inferred from the nearly time-invariant relative ion abundances at longer time delays and the observation of reaction in both directions.

The nonobservation of $CH_3OH{\cdot}^{37}Cl^-$ (m/z 69) and $CF_3CO^{37}Cl{\cdot}^{37}Cl^-$ (m/z 171) (Figure 1c) indicates that only chloride ion of the selected mass (35 in this study) can be transferred between the neutrals and that scrambling of isotopic chlorines in $CF_3COCl_2^-$ does not occur. The latter is further confirmed in the continued reaction sequence.

At the same time delay (800 ms) that the mass spectrum shown in Figure 1c is taken, a second double-resonance pulse ejects all ions but $CF_3COCl_2^-$ in which at least one of the two chlorines is ^{35}Cl (Figure 1d). Then, another time delay elapses and the mass spectrum (Figure 1e) is recorded. Here, only $CH_3OH{\cdot}^{35}Cl^-$ but not $CH_3OH{\cdot}^{37}Cl^-$ is observed. Similarly, only $CF_3COCl_2^-$ with at least one ^{35}Cl is present. This indicates that in $CF_3COCl_2^-$ the two chlorines are distinguishable—only the one which originally came from external source, $CH_3OH{\cdot}^{35}Cl^-$, can be passed on to another neutral acceptor. Thus the two chlorines in CF_3COCl_2 are not equivalent. The barrier must be significant considering that some 10 kcal/mol or more unfixed energy is available in the collision complex formed from the chloride donor and acceptor due to ion-dipole interactions.

A similar experimental sequence established that the two chlorine atoms in $Cl_2CO_2CH_3^-$ are also not exchangeable under our experimental conditions.

The results are consistent with our proposal that reaction 1 occurs on a double-well potential energy surface.[1] The two intermediates can best be described as ion-neutral complexes loosely bound by charge-dipole and charge-induced dipole forces, with one chlorine atom covalently bonded to carbon while the other is only attracted to the neutral molecule by electrostatic interactions. The two intermediates, each having one or the other chlorine atom covalently bonded to carbon, are separated by a barrier which is responsible for the observed reaction kinetics.[1] At the top of the barrier is the tetravalent transition state.[1a,c] Although this structure is less stable than the charge-dipole complex, it is clearly more stable than one would expect based on simple thermochemical considerations,[1a,c] suggesting an unusual structure.[1c]

A triple-minimum surface with the tetravalent structure as a global minimum is not precluded by our results, provided that there is a substantial barrier between it and the loose ion-molecule complex. It is not clear, however, why such a barrier should exist. The barrier in our suggested surface arises because the tetravalent structure which is a minimum along one coordinate of the potential energy surface has become a saddle point connecting the more stable, loose ion-molecule complexes.[1a]

In support of our belief that the tetravalent adduct, $RCOCl_2^-$, is not a stable intermediate, we note that Bohme et al. have observed that very stable nucleophiles, F^-, Cl^-, CN^-, and NO_2^-, all failed to produce (covalent) adducts with formaldehyde in a flowing afterglow instrument.[13] They proposed that the very high electron affinities of these nucleophiles may explain their unwillingness to from a tetravalent adduct with a lower electron affinity. More completely, however, it is the overall reaction thermodynamics, which also includes contributions from the newly formed carbon-nucleophile bond, the broken carbonyl π-bond, and rehybridization at the carbon center in addition to change in electron affinities, which determines the feasibility of formation of the adduct.[1a,c]

In summary, all of our experimental evidence suggests that the tetravalent adduct, $RCOCl_2^-$, must be either a transition state or, possibly, an unstable intermediate (in the case of a three-minima surface). While our model reaction potential energy surface consists of two minima, any more complicated surface, for example, one involving three minima,[16,17] cannot be precluded based on currently available experimental evidence. For reactions with other nucleophiles and leaving groups,[2,3,6,7,9,12,13] the surface may be quite different. Thus, in those cases, the tetravalent adduct may be a global minimum.

Acknowledgment. We are grateful to the National Science Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work.

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Acylnitrilium Ion Cyclizations in Heterocycle Synthesis. A Convergent Method for the Preparation of 2-Acylpyrrolines via the Intramolecular Acylation of Silyloxyalkenes with α-Keto Imidoyl Chlorides

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The polycyclic ring system of the alkaloid dendroxine (**1**) has remained a formidable challenge for efficient chemical synthesis.[1] As part of a unified approach to this, and related *Orchidaceae* metabolites, we required a practical synthesis for the pyrroline **3** (Scheme I).[2] Recently we reported the use of silver ion pro-

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(2) Presently, there are very few general methods for the synthesis of Δ^1-pyrrolines. These procedures include the 1,3-dipolar cycloaddition of nitrile ylides[3] and their equivalents[4] to alkenes, the intramolecular alkylation of metalloimines,[5] and the anionic condensation of vinylogous amides with vinyl sulfonium salts.[6]
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Scheme I

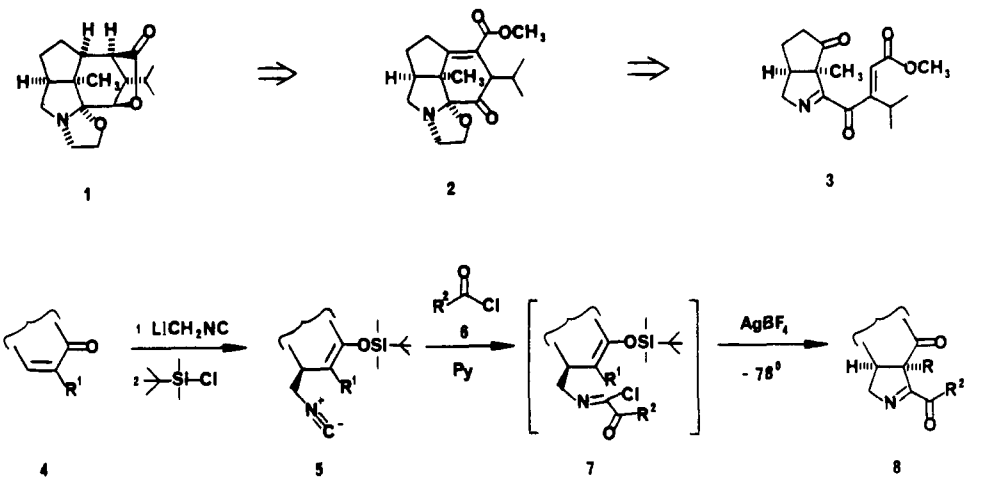
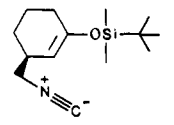
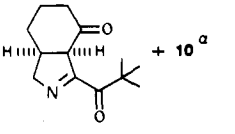
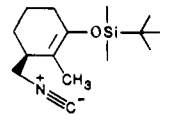
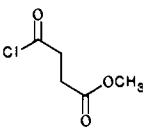
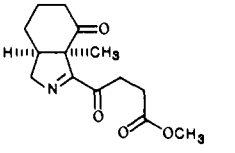
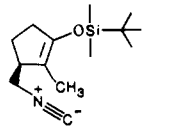
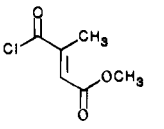
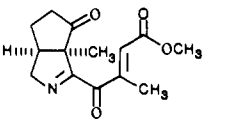
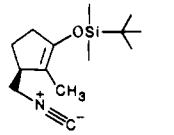
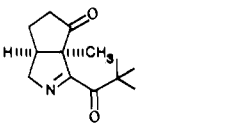
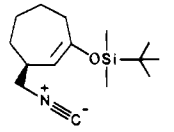
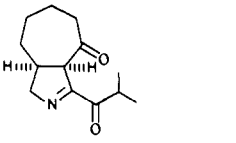
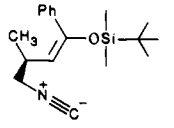
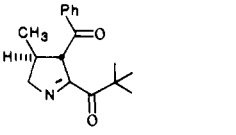


Table I. Pyrroline Synthesis via Intramolecular Imidoyl Chloride Acylations

	isonitrile **5**	acyl chloride **6**	pyrroline **8**	yield, %
a			 1:1.6	61
b				62
c				67
d				64
e				59
f				69

[a] In this instance, partial conversion of the Δ'-pyrroline into its Δ²-isomer occurred rapidly.[13]

moted acylnitrilium ion–arene cyclizations for the construction of the erythrinane skeleton as well as a variety of representative azacycles.[7,8] We now describe a convergent synthetic approach to 2-acylpyrrolines (e.g., **4** → **8**) which relies on the use of silylenol ethers as nucleophilic addends in acylnitrilium ion cyclizations. In addition, we have determined that simple nonactivated alkenes readily participate in acylnitrilium ion initiated heteroannulations.

The substrate isonitriles **5a–f** which were utilized in this study were prepared as previously described[9] by the exposure of the corresponding enones **4** to lithiomethyl isocyanide[10] (THF–HMPA, −78 °C) followed by silylation (*t*-BuMe$_2$SiCl, −78 → 25 °C). The selective conversion of the isonitriles **5** into the requisite α-keto imidoyl chlorides **7** was found to be rather sensitive to the conditions used for acylation.[11] It was ultimately determined that the acylation of these sensitive isonitriles could be conveniently achieved by their exposure to acyl chlorides in the presence of

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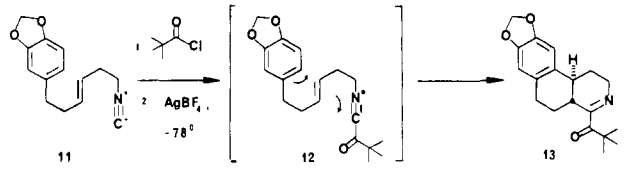
pyridine (1 equiv) over 1-3 h. The cyclization of the unpurified α-keto imidoyl chlorides **7a-f** to the pyrrolines **8a-f** was readily accomplished in the presence of $AgBF_4$ (1.1 equiv) under high dilution in CH_2Cl_2-$ClCH_2CH_2Cl$ at -78 °C.[12,13] It is noteworthy that the removal of the pyridine buffer prior to the cyclization of the intermediates **7a-f** was determined to be unnecessary. A summary of results obtained from a comprehensive series of $AgBF_4$-promoted acylnitrilium ion-silylenol ether cyclizations appears in Table I.

We have previously noted that acylnitrilium ions are sufficiently electrophilic to undergo facile cyclization with nonactivated arenes at -20 °C.[8] The use of *simple* alkenes as nucleophilic addends in acylnitrilium ion initiated heteroannulations would be of considerable synthetic interest. To explore this possibility, the unsaturated isonitrile **11** was sequentially acylated ($(CH_3)_3CCOCl$, 25 °C, 6 h) and then subjected to $AgBF_4$-mediated cyclization (CH_2Cl_2-CH_3NO_2, -78 °C). As had been desired, the tetrahydropyridine **13** was obtained as the major cyclized product in 53% isolated yield.[14] The extension of this methodology to the synthesis of naturally occurring ring systems is under current pursuit.

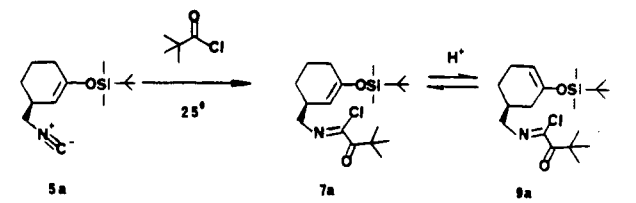


The examples presented above clearly indicate the utility of acylnitrilium ion initiated cyclizations for the synthesis of polyfunctional azacycles. The use of these cations in hetero-[4 + 2] cycloaddition reactions as well as the application of the present methodology to the synthesis of the *Orchidaceae* alkaloids will be reported in due course.

Acknowledgment. Support for this research by a grant from the National Institutes of Health is gratefully acknowledged. This communication is dedicated to the memory of Professor Robert V. Stevens.

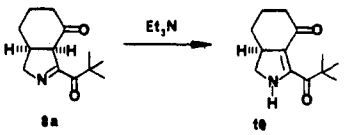
Supplementary Material Available: Representative experimental procedure for the synthesis of a 2-acylpyrroline (1 page). Ordering information is given on any current masthead page.

(11) Prolonged exposure of the substrate **5a** to trimethylacetyl chloride (e.g., 4-7 h, 25 °C) in the absence of pyridine led to the formation of the anticipated adduct **7a** along with its positional isomer **9a** (**7a**/**9a** = 1/1). The formation of **7a** and its subsequent conversion to **9a** was conveniently monitored by 300-MHz NMR spectroscopy. The isomerization of the silylenol ether function under these conditions is attributable to trace amounts of HCl present in the reaction medium.



(12) Several alternative procedures intended to bring about the cyclization of the adducts **7a-f** [e.g.: $Bu_4N^+F^-$ (THF, -78 °C), AgF (CH_3CN, -30 → 25 °C), and $SnCl_4$ (CH_2Cl_2, -78 → 0 °C)] gave lower yields of the desired pyrrolines.

(13) The Δ^1-pyrroline **8a** was found to undergo facile tautomerization to its Δ^2-isomer upon exposure to amine bases or silica gel. Accordingly, treatment of the crude pyrroline **8a** with triethylamine (1 equiv) immediately following cyclization provided the Δ^2-pyrroline **10** in 71% chromatographed yield.



(14) Evidence for the existence of a trans-fused B, C ring junction in **13** was provided by 300-MHz COSY experiments. A definitive assignment awaits single crystal X-ray structure determination.

Intrastrand Bis(guanine) Chelation of d(CpGpG) to *cis*-Platinum: An X-ray Single-Crystal Structure Analysis

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The antitumor drug *cis*-diamminedichloroplatinum(II) (*cis*-$PtCl_2(NH_3)_2$, abbreviated as *cis*-Pt) is known to bind preferentially to neighboring guanines in the DNA, both in vitro and in vivo.[1-7] This has initiated studies-mainly by NMR-on *cis*-Pt interactions with CG-containing oligonucleotides.[8-15] Recently, Lippard et al.[16] succeeded in solving the crystal structure of *cis*-$Pt(NH_3)_2$-[d(pGpG)-*N*7(1), *N*7(2)], which appears to be hardly different from the predicted structure in solution.[17] Since the stacking properties of the neighboring bases on the GG chelate could be important, we started studies on the precise structure of platinated trinucleotides that contain a d(GpG) sequence.

In this paper, the preliminary results of an X-ray structure determination of *cis*-$Pt(NH_3)_2$[d(CpGpG)-*N*7(2),*N*7(3)] are reported. The synthesis of the trinucleosidediphosphate[18] d(CpGpG) and the stoichiometric reaction of this DNA fragment with *cis*-Pt[19] have been described elsewhere. Two types of single crystals[20] were obtained.[21] Because the crystal form II showed

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(20) The crystals were grown by vapor diffusion from aqueous solutions containing 12.5% 2-methyl-2,4-pentanediol (2-MPD) and 10 mM of the compound at pH 8.1, which are in equilibrium with a reservoir which contains a 0.1 M HAc/KAc buffer solution and 25% 2-MPD (+H 5.7).

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