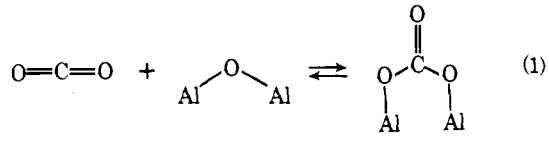
connected by weak (>2.1 Å) Mo-O bonds to opposite sides of an Mo_4O_{12} ring, yielding the structural formula[10] $(H_2CO_2^{2-})(OH^-)(Mo_4O_{12})$. From this point of view, the $CH_2Mo_4O_{15}H^{3-}$ anion is seen to be an acetal derivative. The C-O distance of 1.393 (9, 9, 9, 2) Å[11] and the O-C-O angle of 115 (1)° are accordingly in good agreement with the corresponding values of 1.382 (4) Å and 114.3 (7)° in dimethoxymethane.[12]

If one considers the $CH_2Mo_4O_{15}H^{3-}$ anion to be an aldehyde adduct, the H_2CO binding site can be viewed as an acid-base pair site consisting of two coordinatively unsaturated molybdenum centers and a basic oxygen atom. In this sense, the mode of H_2CO binding conforms to current models for substrate binding on solid oxide surfaces.[13] There is, however, at present no spectroscopic evidence which indicates that aldehydes form surface acetals upon interaction with oxide surfaces. Unfortunately, the characteristic C-O IR absorptions for compound **1** and its analogues fall in the 990-1100-cm^{-1} range usually obscured by oxide lattice absorptions, and their IR spectroscopic observation would in many cases be difficult.[14] IR studies of the interaction of CO_2 with α-alumina have provided strong evidence for surface binding of the closely related type shown in eq 1.[15] It is therefore not unreasonable



(1)

to predict that H_2CO should interact in a similar fashion when suitable acid-base pair binding sites are available.

The formation of acetal molybdates such as compounds **1** and **2** appears to be quite general. Hydrated acetaldehyde, benzaldehyde, and trifluoroacetaldehyde all react with $[(n\text{-}C_4H_9)_4N]_2Mo_2O_7$ to form derivatives $RCHMo_4O_{15}H^{3-}$ as tetrabutylammonium salts.[16] Attempts to synthesize ketal derivatives $R_2CMo_4O_{15}H^{3-}$ have thus far been unsuccessful. Reaction of hydrated acetone or hexafluoroacetone with tetrabutylammonium dimolybdate, for example, yields α-$[(n\text{-}C_4H_9)_4N]_4Mo_8O_{26}$ as the major product. Apparently, enolate and fluoroform formation prevail in the presence of the basic dimolybdate ion. We are currently examining these reactions in greater detail.

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(5) The ^1H NMR spectrum of 1 in CD_2Cl_2 at 25 °C displays only free acrolein, water, and counterion resonances >5 min after dissolution.
(6) Prepared by reacting excess formaldehyde hydrate with $[(n\text{-}C_4H_9)_4N]_2Mo_2O_7$ in CH_2Cl_2 at 25 °C and adding ether to obtain crude product.
(7) Observed from KBr pellets at 1078 and 990 cm^{-1} for 1 and at 1075 and 1006 cm^{-1} for **2**. An isotope shift of ~15 cm^{-1} was observed for ^{18}O enriched **2**.
(8) Large, well-shaped single crystals of **2** obtained as described above are monoclinic, space group $P_{21/n}$ (an alternate setting of $P_{21/c}$-C_{2h}^5, No. 14) with a = 17.066 (2), b = 16.469 (3), c = 28.420 (4) Å; β = 123.62 (1)°; and Z = 4. Three-dimensional X-ray diffraction data (15 237 independent reflections having $2\theta_{MoK\bar{\alpha}} < 55°$) were collected on a computer-controlled four-circle Syntex $P\bar{1}$ autodiffractometer using graphite-monochromated Mo $K\bar{\alpha}$ radiation and full (1° wide) ω scans. The four molybdenum atoms of the totally general-position asymmetric unit were located using direct methods (MULTAN); the remaining anionic and cationic nonhydrogen atoms and the anionic hydrogen atoms were located by standard difference Fourier techniques. The resulting structural parameters have been refined to convergence (R = 0.042 for 6343 independent reflections having $2\theta_{Mo\ K\bar{\alpha}} < 43°$ (the equivalent of 0.50 limit Cu $K\bar{\alpha}$ sphere) and $I > 3\sigma(I)$) using unit-weighted full-matrix least-squares techniques with anisotropic thermal parameters for all 71 nonhydrogen atoms and isotropic thermal parameters for the 3 anionic hydrogens. Refinement is continuing with those reflections having $2\theta_{Mo\ K\bar{\alpha}} < 55°$ and a model which includes isotropic cationic hydrogen atoms.
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(18) Fellow of the Alfred P. Sloan Foundation, 1976-1978.

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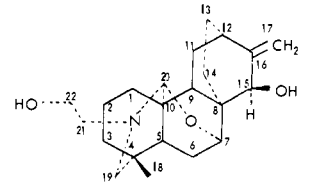
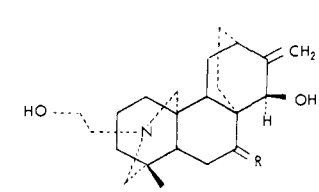
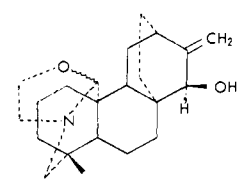
An Unusual Rearrangement of Ajaconine: An Example of a "Disfavored" 5-Endo-Trigonal Ring Closure

Sir:

The structure of ajaconine (**1**), the major alkaloid of the seeds of *Delphinium ajacis* and *D. consolida*, was established elegantly by Dvornik and Edwards[1,2] and was correlated[3] subsequently with the known alkaloid atidine (**2**). Ajaconine was the first example of a C_{20}-diterpenoid alkaloid bearing an internal carbinolamine ether linkage (N-C-O-C) between C(7) and C(20). This communication reports an unusual rearrangement of ajaconine via a "disfavored" 5-endo-trig ring







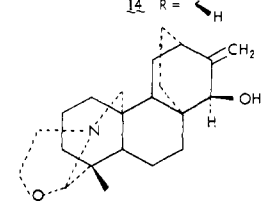


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Table I. Carbon-13 Chemical Shifts and Assignments for Ajaconine (**1**), Ajaconium Chloride (**10**), Atisinium Chloride (**12**), Dihydroajaconine (**14**), 7α-Hydroxyisoatisine (**13**), and Isoatisine (**4**)[a]

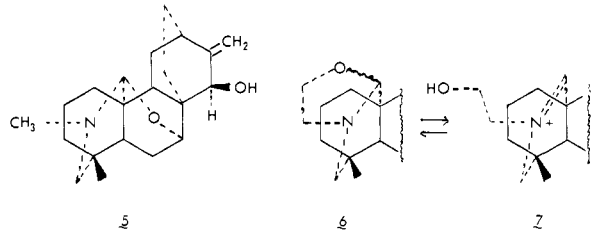
carbon	1[b]	1[c]	10[d]	12[d]	14[b]	13[b]	4[b]
1	41.3	42.4	42.6	42.7	39.8	40.3	40.6
2	21.1	22.0	21.1	21.5	23.1	22.0	22.1
3	40.3	41.1	37.3	37.6	41.1	39.6	40.0
4	33.6	34.5	35.2	35.4	33.5	38.1	38.1
5	44.4	45.4	44.8	46.6	47.9	46.4	48.6
6	25.1	27.4	20.6	21.2	20.6	20.7	19.2
7	75.5	76.3	70.7	32.5	70.4	70.6	31.9
8	41.6	42.9	44.3	39.4	42.6	42.6	37.5
9	37.0	38.3	41.3	41.8	39.5	39.6	39.6
10	35.4	36.5	48.1	48.6	38.0	35.7	35.9
11	30.1	31.2	29.6	29.9	28.1	28.4	28.1
12	26.8	27.9	36.4	36.8	36.1	36.2	36.4
13	27.0	27.9	29.6	27.6	26.4	28.3	27.6
14	26.6	26.4	26.8	27.2	25.4	25.5	26.4
15	72.2	73.5	72.2	77.2	71.9	71.9	76.8
16	157.3	157.2	156.5	156.8	156.0	155.8	156.2
17	108.0	108.0	112.9	112.5	110.1	110.1	109.2
18	25.3	25.5	26.2	26.3	26.5	24.3	24.3
19	51.7	54.0	66.2	66.1	60.2	98.3	98.4
20	87.8	89.7	184.7	185.5	53.9	49.5	49.8
21	57.3	58.3	61.5	61.7	58.0	54.9	54.9
22	58.0	60.0	59.8	59.8	60.7	58.8	58.6

[a] Chemical shifts in parts per million downfield from Me_4Si. [b] Solvent deuteriochloroform. [c] Solvent deuteriomethanol. [d] Solvent D_2O.

closure to a new, oxazolidine ring-containing compound, 7α-hydroxyisoatisine (**13**).

Compounds containing the oxazolidine ring or a carbinolamine group with the oxygen on C(20) are known to rearrange[4] to isomeric compounds with a C(19) oxygen by treatment with methanolic alkali or even by simple refluxing in methanol, e.g., atisine (**3**) → isoatisine (**4**), veatchine → garryine, and garryfoline → isogarryfoline. An attempt to rearrange ajaconine (**1**) resulted in a mixture[2,5] and the related *N*-methyl C(7)–C(20) ethers; e.g., compound **5** failed to isomerize under these conditions. On the basis of chemical reactions and hydrogen-interaction theory, the Canadian workers concluded[2] that a driving force for the rearrangement in the internal carbinolamine ethers (e.g., ajaconine and other related compounds) is absent. They also mentioned that an entropy factor must favor the internal ether over the oxazolidine ring and thus the C(7)–C(20) ethers should be more stable than the oxazolidine derivatives.

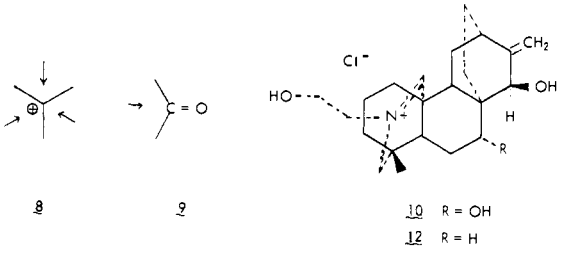
The oxazolidine ring systems present in many C_{20}-diterpenoid alkaloids (e.g., **6**) are in equilibrium in ionic solvents with the quaternary immonium salts (**7**) and consequently are very strong bases.[6] The quaternary immonium salts (**7**) are poorly structured vectorially for cyclization to the oxazolidines (**6**). Such a ring closure according to Baldwin's rules for cyclization is "disfavored". Experimental evidence[6] demonstrates, however, that an equilibrium exists between **6** and **7**. It therefore



5 **6** **7**

appears that the Baldwin rules are less prohibitive for quaternary immonium salts bearing a full charge on the nitrogen. These salts resemble carbocations to a greater extent than uncharged groups. Clearly an attack on a carbocation ion (**8**) must exhibit less vectorial specificity than an attack on, say, a carbonyl group (**9**). Because the quaternary immonium salts (**7**) are intermediate between an uncharged group and a carbocation, the equilibrium **6** ⇄ **7** is probably slower than a ring closure which is not disfavored.

Ajaconine forms an immonium salt[7] (ajaconium chloride, **10**) instead of a protonated-type (+NH) salt by treatment with HCl. Treatment of ajaconium chloride with base regenerates ajaconine (**1**) instead of possible compound **11** (7α-hydroxy atisine) which would parallel the formation of atisine (**3**) from atisinium chloride (**12**). When the ^{13}C NMR spectrum of



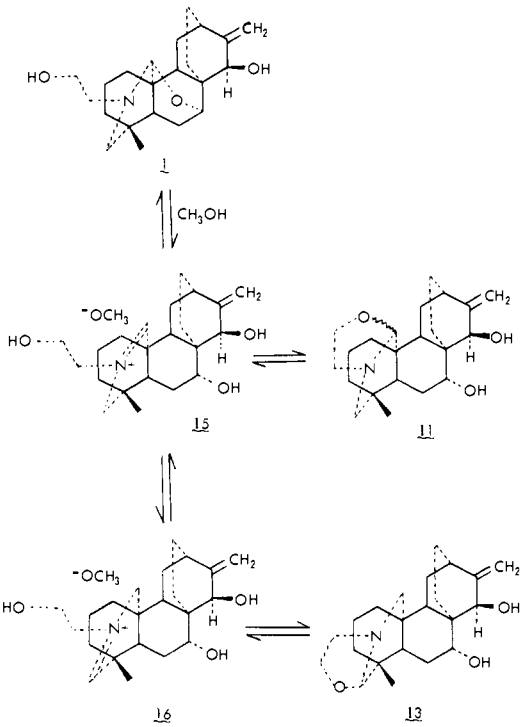
8 **9** **10** R = OH **12** R = H

ajaconine was taken in CD_3OD the chemical shifts of carbons 7, 19, 20, 21, and 22 along with other chemical shifts had moved downfield in comparison with the spectra taken in $CDCl_3$, Me_2SO, or acetone (Table I). A similar effect was observed in the ^{13}C NMR spectrum of ajaconine in a solution of D_2O and CD_3OD. This effect was observed only in ionic solvents.[8] These results indicate that in hydrogen-bonding-type solvents the ether linkage of ajaconine ionizes and covalent solvation takes place. This observation accounts for the high pK_a value of ajaconine in an aqueous solution and the formation of immonium salts. A similar phenomenon had been observed earlier in the case of atisine (pK_a = 12.5) and related alkaloids.[6]

Refluxing ajaconine (**1**) in methanol or aqueous methanol afforded a new compound[9] identified as 7α-hydroxyisoatisine (**13**): $C_{22}H_{33}NO_3$, *m/e* 359.5; mp 118–122 °C; $[\alpha]^{24}_D$ −16.3° (*c* 1.05 in $CHCl_3$); IR (KBr) 3375 (OH), 1660 and 900 (>C=CH_2) cm^{-1}. The ^1H and ^{13}C NMR spectra of **13** are very similar to those of isoatisine.[10,11] Reduction of 7α-hydroxyisoatisine with $NaBH_4$ in 10% aqueous methanol afforded dihydroajaconine (**14**). Formation of **13** demonstrates the cleavage of the C(7)–C(20) ether linkage and formation of an oxazolidine ring. When ajaconine was refluxed with

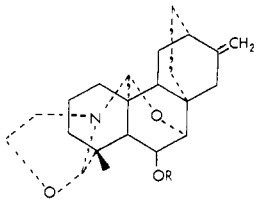
deuterated methanol under a nitrogen atmosphere, a mixture of C(19),(20)-deuterated ajaconine and C(19),(20)-deuterated 7α-hydroxyisoatisine was formed. This deuteration experiment indicates that ajaconine ionizes and rearranges to 7α-hydroxyisoatisine (**13**) and that these two species are in equilibrium in refluxing methanol. The mechanism for the rearrangement may now be considered.

The species **15** closes to ajaconine (**1**) and not to **11** because the closure **15** → **11**, being partially disfavored, is much slower than the closure **15** → **1**. However, the species **15** should undergo an isomerization (**15** → **16**) which has a precedent in the veatchine → garryine and the atisine (**3**) → isoatisine (**4**) isomerization. The species **16** should readily close now to the oxazolidine (**13**), in spite of the closure being *partially disfavored because there is no faster process in competition with this ring closure.*



The rearrangement of ajaconine (**1**) into 7α-hydroxyisoatisine (**13**) represents an unusual example of a Baldwin rule "disfavored" 5-endo-trig-ring closure. On the basis of the above results we conclude that the ether linkage of ajaconine ionizes in ionic solvents and that ajaconine rearranges via a disfavored 5-endo-trig process to an isooxazolidine ring containing compound.

Because of the unusual character of the C(7)–C(20) ether system in ajaconine, it would be interesting to examine the behavior of the spiradine-type alkaloids (**17, 18**)[12] in ionic solvents to determine what rearrangement products are formed and to see which ether linkage forms an immonium salt.



17 R = Ac Spiradine F
18 R = H Spiradine G

Acknowledgment. We acknowledge the contributions of Professor K. Wiesner to this paper. His referee's report provided an interpretation of the behavior of the internal carbinolamine ethers which we have adopted in the revision of this paper. We thank Mr. Howard C. Higman of the Tobacco and Health Laboratory, USDA-ARS, Richard Russell Research Center, Athens, Ga. for the mass spectrum and Dr. Rajinder Sawhney for isolation of a sample of ajaconine.

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(7) The ^{13}C NMR spectrum of ajaconine hydrochloride in D_2O was compared with the spectrum of atisinium chloride to confirm its structure as **10**.
(8) These downfield shifts do not result from ordinary solvent effects; e.g., examination of dihydroajaconine shows essentially the same chemical shifts in either CD_3OD or $CDCl_3$.
(9) In a typical experiment, 100 mg of ajaconine in 10 mL of CH_3OH was refluxed over a steam bath for 1.5 h to achieve 60% rearranged product **13**. The rate of conversion depends upon the concentration.
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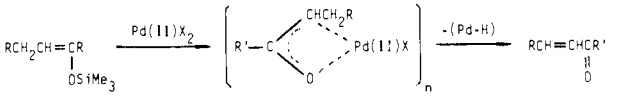
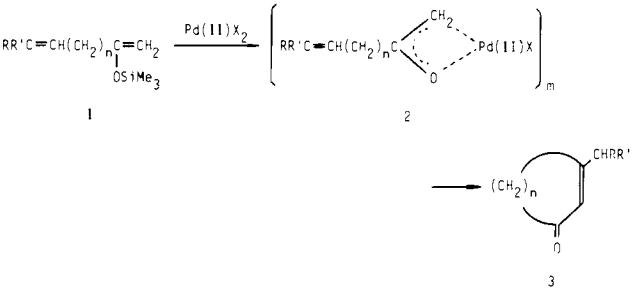
Cyclization Reactions via Oxo-π-allylpalladium(II) Intermediates

Sir:

In the previous paper[1] we reported Pd(II) assisted dehydrosilylation[2] of silyl enol ethers leading to α,β-unsaturated carbonyl compounds, in which oxo-π-allylpalladium(II) complexes were proposed as key intermediates. In support of the reaction mechanism involving the oxo-π-allylpalladium(II) intermediate, we[3] recently succeeded in the isolation of a stable 2-*tert*-butyl-π-oxopropenylpalladium(II) complex in the reaction of silyl enol ether of pinacolone with $Pd^{II}Cl_2(PhCN)_2$.



Herein, we report Pd(II) promoted intramolecular cyclization of silyl enol ethers (**1**) of alkenyl methyl ketones to produce cyclic α,β-unsaturated ketones (**3**), in which oxo-π-allylpalladium(II) complexes (**2**) may be involved as key intermediates.



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