glycosidic linkages to the aglycon was obtained by subjecting **1** to ozonolysis followed by reduction with sodium borohydride to give **16** and **17**.[3]

Finally as a consequence of knowing the absolute stereochemistry of sugar A (L) and the nature of the glycosidic linkage to the aglycone (α),[15] as well as the relative stereochemical environment at C_8, C_9 and C_{10},[14] we were able to deduce the absolute stereochemistry of kijanimicin (**1**) from the observed glycosylation shifts in the ^{13}C NMR spectra in going from **3** to **1**. Thus the observed deshielding at C_9 (+8.4) coupled with the shielding at C_8 (−0.7) and absence of any shielding at C_{10} were in excellent agreement with the expected glycosylation shifts for an α-L-deoxysugar glycosidically attached to an aglycone having the stereochemical features present at C_8, C_9, and C_{10} in **1**.[14] It therefore follows that C_9 has the *S* configuration. Had the configuration at C_9 been *R*, then marked shielding would have been predicted at C_8, C_9, and at C_1 for sugar A[13,14] which was not the case.

It is therefore concluded that the total structure and absolute stereochemistry of kijanimicn may be represented by **1**. Kijanimicin (**1**) has antitumor activity and is active against *P.acnes* and is a member of a new class of tetronic acid containing antibiotics of which the tetrocarcins[12,16–18] and antlermicins[19,20] are the only other known members. The latter differ in the structure of the aglycon as well as in the structures of some of the glycosidic components, and full structures for these antiobiotics have not yet been published.

Supplementary Material Available: Table of positional parameters for the nonhydrogen atoms in **10** (2 pages). Ordering information is given on any masthead page.

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Electron-Impact-Induced Fragmentation of Quaternary Ammonium Cations

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Recently Stoll and Röllgen as well as Cotter and Yergey have shown that tetraalkylammonium salts are evaporated and dissociated to yield the corresponding quaternary ammonium cation by simply heating the sample,[1] whereas Lee et al. proposed that electron impact is necessry to cause dissociation of gaseous quaternary ammonium salts to give the corresponding ammonium cation.[2] These reports prompted us to present our recent results on in-beam EI (desorption from extended probes) mass spectrometry[3] of these compounds. The series tetraethyl-, tetrapropyl-, tetrabutyl-, and tetrapentylammonium bromide was selected as typical and studied by the techniques of in-beam EI mass spectrometry and mass-analyzed ion kinetic energy spectrometry (MIKES) or the direct analysis of daughter ions (DADI).[4] Our results are summarized as follows:

Table I. MIKES and IKES of Tetraalkylammonium Cation

R	transition[a]	fragment ion (m/z)	E/E_0[b]	V/V_0[c]
Et	1	102 (a)	0.781	1.275
	2	101 (b)	0.776	1.288
	3	100 (c)	0.766	1.301
	4	86 (d)	0.659	*e*
Pr	1	144 (a)	0.774	1.290
	2	143 (b)	*d*	1.300
	3	142 (c)	0.762	1.309
	4	114 (d)	0.611	1.633
	5	43 (f)	0.229	*e*
Bu	1	186 (a)	0.768	1.302
	2	185 (b)	*d*	1.306
	3	184 (c)	0.761	1.314
	4	142 (d)	0.588	1.703
	5	57 (f)	0.233	*e*
Pn	1	228 (a)	0.765	1.307
	2	227 (b)	*d*	1.311
	3	226 (c)	0.757	1.317
	4	170 (d)	0.570	*e*

[a] See Figure 1. [b] MIKES of tetraalkylammonium cation. [c] IKES obtained by acceleration voltage scanning (V_0 = 1 kV). [d] Overlapping peaks. [e] No data obtained.

(i) When the compound was loaded on a metal tip and inserted into the hot ion source (ca. 280 °C) and heated to 350 °C by the sample heater, or the compound was deposited on an unactivated FD wire of 10-μm diameter tungsten and quickly heated, only the corresponding tetraalkylammonium cation was recorded. Without an electron beam, no fragment ions were detected. This observation is consistent with that of Röllgen or Cotter and not with the results of Lee et al.

(ii) Then the electron beam (filament) was turned on and the in-beam EI spectra were recorded. A significant increase in the abundance of the quaternary ammonium cation was observed, which appears to be consistent with the observation of Lee et al. Two possible explanations are proposed for this increase: (a thermal dissociation of gaseous neutral molecules such as $(R_4N^+X^-)_n$ to the cation R_4N^+ on the hot surface[5] or (b) dissociation induced by electron bombardment.[2] Both processes are conceivable, but from observations at different positions of the tip relative to the electron beam, process b appears to be the major contributing factor. The in-beam EI spectrum of tetrabutylammonium bromide is shown in Figure 1 as a typical example. In addition to these peaks, weak but remarkable cluster ions were observed at m/z 563, 565 $[(R_4N^+)_2Br^-]^+$ and m/z 320, 322 $(R_4NBr - H)^+$. The major spectral features are very similar to those obtained by field desorption,[6] ^{252}Cf plasma desorption,[7] laser desorption,[7] and flash desorption.[2] If quaternary ammonium salts undergo thermal decomposition prior to electron impact[8] or chemical ionization[9] in the ion source as hitherto believed, fragment ions observed in this study are considered to be produced by electron-impact ionization of thermally degraded products such as tributylamine. However, the in-beam EI spectra exhibit very weak peaks corresponding to the molecular ion of butyl bromide,

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(1) Stoll, R.; Röllgen, F. W. *J. Chem. Soc., Chem. Commun.* **1980**, 789. Cotter, R. J.; Yergey, A. L. *J. Am. Chem. Soc.* **1981**, *103*, 1596.

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(4) A Varian 311A double focusing mass spectrometer or a Finnigan 4023T GC/MS/DS quadrupole instrument was used.

(5) Thermal decomposition of tetraalkylammonium cation on hot surfaces has been observed by Röllgen (Röllgen, F. W., private communication, 1980) and Ohashi et al. (Ohashi, M.; Tsujimoto, K.; Funakura, S., unpublished work).

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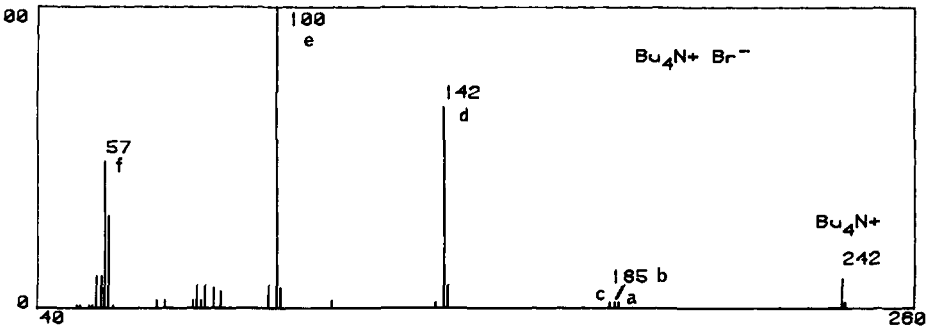

Figure 1. In-beam EI spectrum of tetrabutylammonium bromide (80 eV).

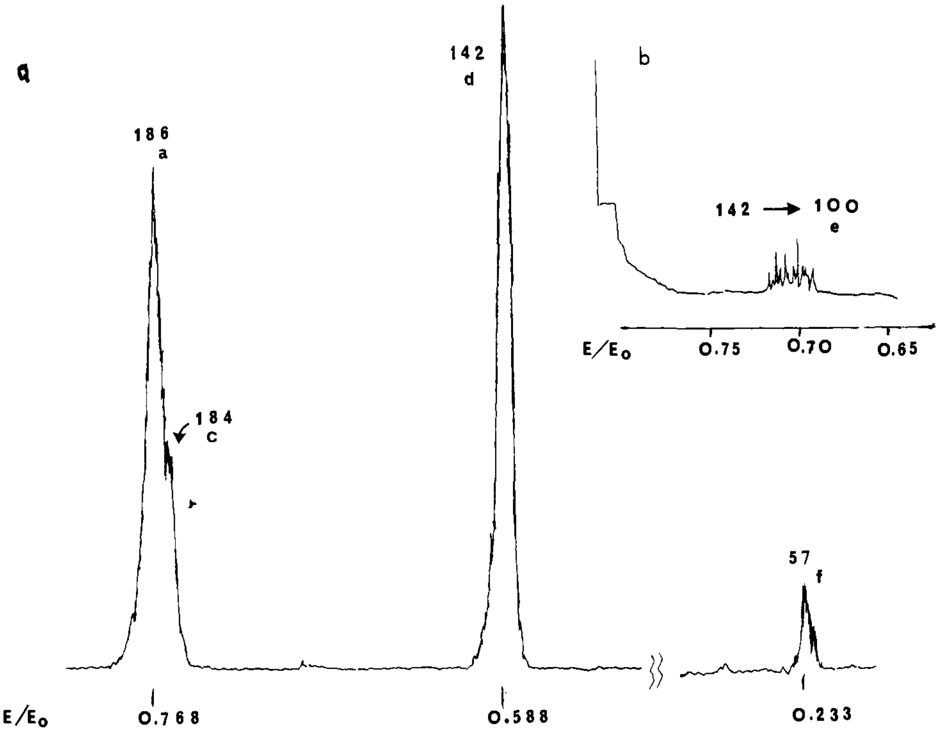

Figure 2. MIKE spectra of tetrabutylammonium cation: (a) metastable transitions from Bu_4N^+; (b) a metastable transition leading to the base peak (m/z 100) from ions at m/z 142.

a thermal degradation product, which were observed in the conventional EI spectrum of the salt. In addition, relative abundances of fragment peaks at m/z 185, 142, and 100 are quite different from those observed in the EI spectrum of tributylamine, another thermal degradation product. These facts suggest that while the contribution of thermal degradation products cannot be discounted, the major peaks of the in-beam EI spectrum are also derived by direct fragmentation of R_4N^+ upon electron impact.

(iii) Furthermore, MIKES[10] confirmed the direct formation of some fragment ions from the R_4N^+ cation. The results are shown in Figure 2 and Table I. Five transitions were commonly observed. In the case of tetraethyl derivative, a metastable transition producing R_3NH^+ from R_4N^+ was weak and two peaks corresponding to the transition leading to $R_3N^{+}\cdot$ and $R_2N^+{=}CHR'$ were clearly observed. In the other three cases the transitions leading to $R_3N^{+}\cdot$ from R_4N^+ were not clear because of three overlapping transitions for $R_3N^{+}\cdot$, R_3NH^+, and $R_2N^+{=}CHR'$ from R_4N^+. All compounds showed abundant transitions leading to $R_2N^+{=}CH_2$ from R_4N^+. Since the trialkylamine molecular ion undergoes the reaction, $R_3N^{+}\cdot \rightarrow R_2N^+{=}CH_2$, quite efficiently,[11] the formation of $R_2N^+{=}CH_2$ ions from R_4N^+ proceeds either through $R_3N^{+}\cdot$ or by concerted direct processes. All major peaks in the in-beam EI spectrum of tetrabutylammonium bromide (Figure 1) were characterized by the MIKES technique.[12]

(iv) In order to clarify the ambiguous processes in MIKES due to overlapping or unresolved peaks, particularly for the process $R_4N^+ \rightarrow R_3N^{+}\cdot + R\cdot$, ion kinetic energy spectra (IKES) were obtained by acceleration voltage scanning to attempt to determine the parent ions of certain daughter ions.[10] The results are summarized in Table I. The parent ions of $R_3N^{+}\cdot$, corresponding to the molecular ions of trialkylamine (a possible thermal degradation product), were clearly shown to be derived by electron-impact-induced fragmentation from the tetraalkylammonium cation, R_4N^+. Interestingly, at least part of the abundance of R_4N^+ was demonstrated to be derived from the cluster ion $[(R_4N)_2Br]^+$ $V/V_0 = 2.329$. The ion d was also shown to be derived from two species: R_4N^+ and ion b.

Of course from these data we cannot exclude contribution of thermal decomposition products to the in-beam spectra. However, we can conclude safely that the following reactions take place commonly in the second field-free region in the reversed Nier–Johnson geometry.

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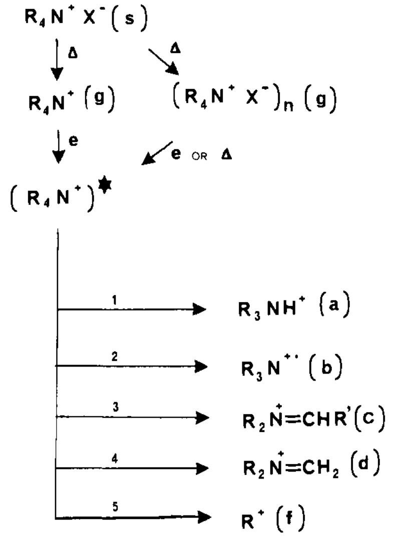
[10] Cooks, R. G.; Beynon, J. H.; Caprioli, R. M.; Lester, G. R. "Metastable Ions"; Elsevier Scientific Publishers: London, 1973; p 42. Maurer, K.; Brunnee, C.; Kappus, G.; Habfast, K.; Schroder, U.; Schulze, P. 9th Annual Conference on Mass Spectrometry, ASMS Committee E-14, Atlanta, GA, May 1971.

[11] Budzikiewicz, H.; Djerassi, C.; Williams, D. H. "Mass Spectrometry of Organic Compounds"; Holden-Day: San Francisco, 1967; Chapter 8.

[12] The MIKES technique established the following two transitions in the in-beam EI fragmentation of Bu_4N^+: E/E_0 0.770; m/z 185 → 142; 0.578 (br); m/z 100 → 58.



Since the parent ions (R$_4$N$^+$) have considerably long lifetimes (ca. 10^{-4}–10^{-5} s, metastable window region) they cannot be electronically excited but only vibrationally excited[13] and are closely related to active species obtained by laser desorption, secondary ion mass spectrometry,[14] plasma desorption, and field desorption (collision-induced dissociation) of these compounds. Although quaternary ammonium cations have hitherto been believed to decompose before evaporation, our results indicate clearly that they survive in a gas phase, are excited into higher vibrational states upon electron impact, and then decompose to give the fragment ions. We believe our results are the first reported examples of electron-impact-induced fragmentation of quaternary ammonium salts.

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Nickel-Promoted Cyclization/Carbonylation in the Preparation of α-Methylene γ-Lactones: Stereospecific Synthesis of (±)-Frullanolide

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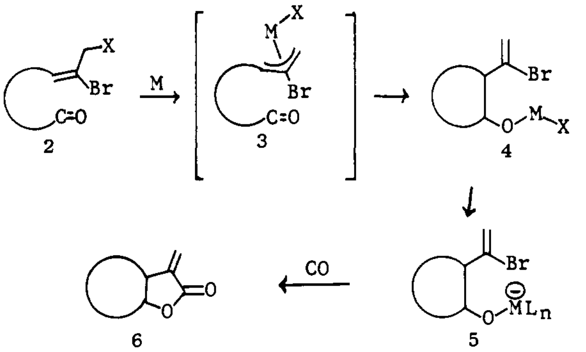
The biological activity of compounds containing the α-methylene lactone group has prompted vigorous development of appropriate methodology and many specific syntheses of natural examples.[1] The most common strategy relies on modification of a preformed lactone ring, usually by multistep procedures, for introduction of the α-methylene unit. We have been developing methods based on zero-valent metal reagents which promote crucial carbon–carbon coupling reactions and lactone formation and produce the α-methylene lactones directly.[2,3] We have recently reported[4] formation of α-methylene lactones using nickel carbonyl to promote intramolecular alkoxycarbonylation of vinyl halides, extending the method of Corey and Hegedus.[5] Here we report that these developments can be combined into a simple procedure for α-methylene lactone synthesis, where nickel carbonyl brings about two different carbon–carbon coupling steps. The method is sensitive to sterochemical features as evidenced by sterospecific synthesis of the natural α-methylene γ-lactone, frullanolide (**1**).[6]

Scheme I. General Pathway



(1)

The general procedure is summarized in Scheme I. The allylic system in **2** (X = halide or sulfonate ester) can be activated as an allyl–nickel complex (e.g., **3**, M = Ni)[7] and then cyclize with the aldehyde unit to produce **4** (potentially a cis/trans mixture). While the general method is well precedented,[7,8] no example of a (2-bromoallyl)nickel complex has been characterized or employed in additions to carbonyl units. The proposed intermediate **4** would be formed with M = Ni(II). If M = Ni(0) as in **5**, alkoxycarbonylation to give **6** can be expected;[4] however, exchange of Ni(II) and Ni(0) in species such as **4** has not been studied systematically.

A simple test case was examined. The compounds **11** and **13** were prepared in a direct way starting with a Wadsworth–Emmons procedure[9] (89% yield) using 6,6-dimethoxyhexanal (**8**)[10] and the anion from α-bromo-α-phosphonoacetate **7** in dimethoxyethane at 25 °C for 1.5 h to give the isomers **9**. The isomers **9***Z* and **9***E* were separated by medium pressure liquid chromatography[11] (MPLC), although for preliminary studies mixtures of *E* and *Z* isomers were employed. Reaction of **9** with 2.75 mol equiv of diisobutylaluminum hydride provided the allylic alcohols **10** (80–85%) yield. The double-bond geometries are assigned on the basis of an analysis [12] of the ^{1}H NMR spectra of the acrylates **9**. Reaction with phosphorus tribromide and an aqueous isolation procedure converted the alcohols **10** to the allylic bromides **11***E* and **11***Z*. The corresponding methanesulfonate esters (**13***E* and **13***Z*) were obtained in good yield from the hydroxy aldehydes **12** (Et$_3$N, CH$_3$SO$_2$Cl, O °C, CH$_2$Cl$_2$). Most of the optimization experiments for the nickel-promoted cyclization were carried out

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