10), 1180 (M^+, 13), 1018 (70), 1017 ($MH^+ - 164$, 100), 854 (17), 853 ($MH^+ - 2 \times 164$, 28), 690 (13), 689 ($MH^+ - 3 \times 164$, 28), 525 ($MH^+ - 4 \times 164$, 10), 427 (18). FAB-MS of compound **9**: m/z (rel int) 1181 (MH^+, 11), 1180 (M^+, 12), 1018 (70), 1017 ($MH^+ - 164$, 100), 854 (16), 853 ($MH^+ - 2 \times 164$, 27), 690 (13), 689 ($MH^+ - 3 \times 164$, 27), 525 ($MH^+ - 4 \times 164$, 9), 427 (18).

Oxidation of Densicomacin with Sodium Periodate. Densicomacin (10 mg) was treated with $NaIO_4$ (100 mg) in dioxane–water (3:1) (4 mL) for 170 h at room temperature. The reaction product was isolated by preparative TLC (250 μm, 20 cm × 20 cm) with with $CHCl_3$–MeOH (97:3). The major product was pentadecanoic acid (2 mg): HR-EI-MS 242.2239, calcd for $C_{15}H_{30}O_2$ 242.2246; ^1H NMR (500 MHz, $CDCl_3$–CD_3OD), δ 0.79 (t, J = 6.8 Hz, 3 H, H-15), 1.51 (m, 2 H, H-14), 2.14 (t, J = 7.5 Hz, 2 H, H-2). Pentadecanoic acid was reacted with CH_2N_2 to give methyl pentadecanoate: FAB-MS 257 (MH^+, 100); ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3 H, H-15), 1.62 (m, 2 H, H-14), 2.30 (t, J = 7.6 Hz, 2 H, H-2), 3.67 (s, 3 H, RCO_2CH_3).

8-Hydroxyannonacin (3): waxy solid, $[\alpha]_D$ +6.1° (c, 0.12, MeOH); UV(MeOH) λ_{max} 209.5 nm (log ε, 4.22); IR ν_{max} (film) 3421, 1749, 1465, 1404, 1216, 1120, 1080 cm^{-1}; FAB-MS, m/z 613.4772 $(MH)^+$ calcd 613.4679 for $C_{35}H_{64}O_8$+H. EI-MS: see Table II and Scheme I.

8-Hydroxyannonacin trimethylsilyl ether derivative: EI-MS, m/z (rel int) 701 (1), 631 (4), 611 (4), 541 (4), 521 (5), 451 (9), 473 (12), 371 (15), 357 (44), 341 (20), 267 (10), 271 (52), 213 (30).

8-Hydroxyannonacin pentaacetate (10): CI-MS, m/z (rel int) 823 (MH^+, 3), 763 (20), 703 (30); EI-MS, m/z (rel int) 581 (1), 521 (3), 511 (0.1), 461 (2), 451 (0.2), 401 (2), 391 (1), 383 (3), 331 (3), 323 (3), 311 (30), 297 (3), 263 (7), 251 (20), 237 (10), 191 (12), 183 (8), 123 (27). ^1H NMR: see Table IV.

Goniothalamicin (4): white crystals, mp 91–2 °C, $[\alpha]_D$ +10.4° (c, 0.08, MeOH); UV λ_{max}, (MeOH) 209.5 nm (log ε, 3.90); IR ν_{max} (KBr) 3463, 1749, 1479, 1430, 1332, 1119, 1081 cm^{-1}; FAB-MS, m/z 619.4512 (MNa^+), calcd 619.4550 for $C_{35}H_{64}NaO_7$; EI-MS: see Scheme I and Table II. ^1H NMR and ^{13}C NMR: see Table IV.

Goniothalamicin trimethylsilyl ether derivative: EI-MS, m/z (rel int) 585 (2), 515 (6), 495 (7), 425 (64), 405 (4), 369 (6), 385 (20), 335 (8), 299 (34), 213 (40).

Goniothalamicin Tetraacetate (11). Acetylation was carried out with Ac_2O–pyridine and yielded tetraacetate 11: CI-MS, m/z (rel int) 765 (0.2), 705 ($MH^+ - 60$, 19), 645 ($MH^+ - 2 \times 60$, 52), 523 ($MH^+ - 4 \times 60$, 10), 385 ($MH^+ - 3 \times 60$, 34); EI-MS, m/z (rel int) 495 (28), 435 (14), 375 (4), 365 (1.4), 339 (20), 325 (1), 315 (5), 305 (2), 279 (6), 265 (2), 253 (2), 205 (3), 183 (2), 123 (15).

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Supplementary Material Available: ^1H, ^{13}C, and 2D NMR spectra of 1–11 (42 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

$C_5H_9O_2^+$ Ions: The Correlation between Their Thermochemistry in Acidic Solution and Their Chemistry in the Gas Phase

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Each of a series of $C_5H_8O_2$ isomeric carboxylic acids and lactones (1–9) was protonated in both concentrated sulfuric acid and trifluoromethanesulfonic acid. The thermally induced transformations of the protonated species were then studied over the temperature range −40 to +160 °C. As a general rule, all the initially generated cations were eventually converted to protonated γ-valerolactone ($1H_O^+$) and, finally, to protonated cyclopentenone ($10H_O^+$). The cations derived from the cyclopropanecarboxylic acids 7 and 8 both underwent ring opening to the unsaturated cation $6H_O^+$, which then rearranged to a protonated α-lactone. In concentrated sulfuric acid the latter species loses carbon monoxide to afford protonated 2-butanone $11H_O^+$. The CIMS spectra of compounds 1–9 were recorded, allowing a correlation between the fragmentation routes in the gas phase and the transformations observed in solution. In this way, the data obtained in strong acids are used to assign reasonable structures to the gas-phase ions.

Introduction

In previous papers[1,2] we described the protonation of carboxylic acid derivatives in concentrated sulfuric acid, the thermally induced transformations of the resulting ionic species, and finally, the correlation between these transformations and the fragmentation patterns found for the same ions in the gas phase by recording the chemical ionization mass spectra (CIMS) of the corresponding precursors. This work established the feasibility of

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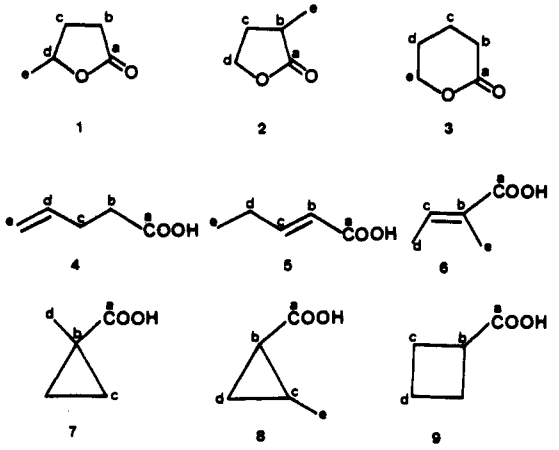
Table I. ^{13}C NMR Data for the Protonated Species

	$1H_O^+$	$2H_O^+$	$3H_O^+$	$5H_O^+$	$6H_O^+$	$7H_O^+$	$8H_O^+$	$9H_O^+$
δ_C[a] (ppm)								
C_a	197.0	199.9	193.0	181.9	182.6	195.8	193.9	195.8
	(19.7)	(19.7)	(21.6)	(9.5)	(8.9)	(12.3)	(12.6)	(13.7)
C_b	32.7	39.4	28.2	112.6	123.6	18.5	22.4	37.8
	(3.5)	(5.2)	(−1.8)	(−7.5)	(−4.5)	(−0.6)	(5.0)	(−0.6)
C_c	28.8	29.6	16.2	175.3	160.8	26.8	31.6	26.0
	(−0.4)	(−1.3)	(−3.1)	(22.0)	(21.2)	(9.0)	(10.2)	(0.6)
C_d	98.2	82.5	21.0	27.5	15.7	18.7	27.2	18.3
	(21.1)	(16.0)	(−1.6)	(2.2)	(1.6)	(0.0)	(9.0)	(−0.3)
C_e	20.2	14.1	81.9	9.5	9.8		17.6	
	(−0.6)	(−1.1)	(12.4)	(−2.2)	(−1.4)		(−0.1)	
$^1J_{C-H}$[a] (Hz)								
C_b	137.4	131.8	130.8	170.4			174.4	141.0
	(1.0)	(−0.4)	(0.2)	(10.0)			(8.2)	(8.5)
C_c	136.5	140.1	133.3	158.4	157.1	169.5	165.7	145.0
	(0.1)	(5.9)	(1.3)	(5.0)	(−0.6)	(6.2)	(−1.1)	(8.3)
C_d	159.9	162.1	130.8	127.2	129.3	132.3	168.6	140.7
	(7.9)	(12.4)	(0.1)	(0.8)	(2.6)	(4.7)	(2.3)	(3.0)
C_e	129.3	132.8	158.4	128.0	123.5		127.9	
	(2.6)	(4.7)	(9.4)	(1.8)	(−4.5)		(0.1)	

[a] In parentheses: $\Delta\delta_{^{13}C}$ and ΔJ_{C-H}. $\Delta\delta_{^{13}C} = \delta_{^{13}C}$ in spectrum of ion − $\delta_{^{13}C}$ in spectrum of uncharged parent. $\Delta J_{C-H} = J_{C-H}$ in spectrum of ion − J_{C-H} in spectrum of uncharged parent.

fruitfully correlating the CIMS data of certain compounds with the results of studies of the thermally induced transformations of the same compounds in highly acid solutions. Thus, knowledge of the ions present in solution permitted the identification of the fragment ions seen in the gas phase and knowledge of the fragmentation pathways observed by CIMS enabled prediction of the fate of the same ions in solution.[3]

Now we wish to report that our methodology yields useful information when applied to the study of a series of isomeric $C_5H_9O_2^+$ ions obtained by protonation of the lactones **1–3**,[4] the unsaturated carboxylic acids **4–6**, and the cycloalkanecarboxylic acids **7–9**. Although at first

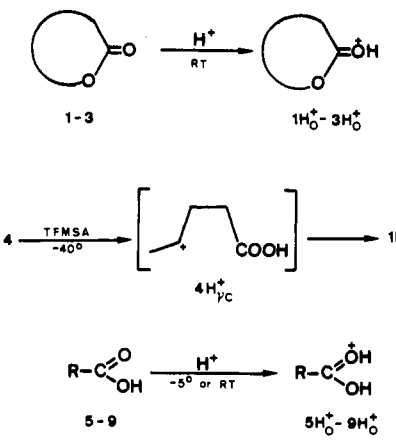


glance the structural diversity within the series suggests dissimilar rearrangement patterns for the thermally activated ionic species, we have found that all of these ions undergo interconversions, either in solution or in the gas phase, and finally converge in the form of O-protonated cyclopentenone ($10H_O^+$).

Results and Discussion

Protonation of Carboxylic Acids and Derivatives 1–9. In general, the protonations were carried out at room temperature by dissolving the carboxylic acid or lactone

Scheme I



in a quantity of either 96% sulfuric acid or neat trifluoromethanesulphonic acid (TFMSA) sufficient to yield a ca. 1 M solution. Except with the acids **4**, **7**, and **8** under such conditions, stable cations in which the proton resided on the carbonyl oxygen were obtained (Scheme I). The ions $7H_O^+$ and $8H_O^+$ were insufficiently stable at temperatures above −5 °C to permit their direct observation. At room temperature, rapid ring opening to the stable O-protonated species $6H_O^+$ took place (Scheme II). Under

Scheme II

$$\mathbf{7}\text{ or }\mathbf{8} \xrightarrow[-5\ ^\circ C]{\text{TFMSA or } H_2SO_4} 7H_O^+ \text{ or } 8H_O^+ \xrightarrow[rt]{} 6H_O^+$$

these conditions, compound **4** underwent C-protonation to yield $4H_{\gamma C}^+$, which then rearranged to the protonated lactone $1H_O^+$. This transformation took place in TFMSA at temperatures as low as −40 °C. ^{13}C NMR data for the ions are summarized in Table I. (For the complementary ^1H NMR data, see the Experimental Section).

As a general rule, the site at which the compounds were protonated at room temperature was the carbonyl oxygen.[5] That this is so is confirmed by the NMR spectra, which show that the carbonyl carbon is deshielded, a result consistent with a contribution by a hydroxycarbenium ion structure to each ion's resonance hybrid. In the protonated

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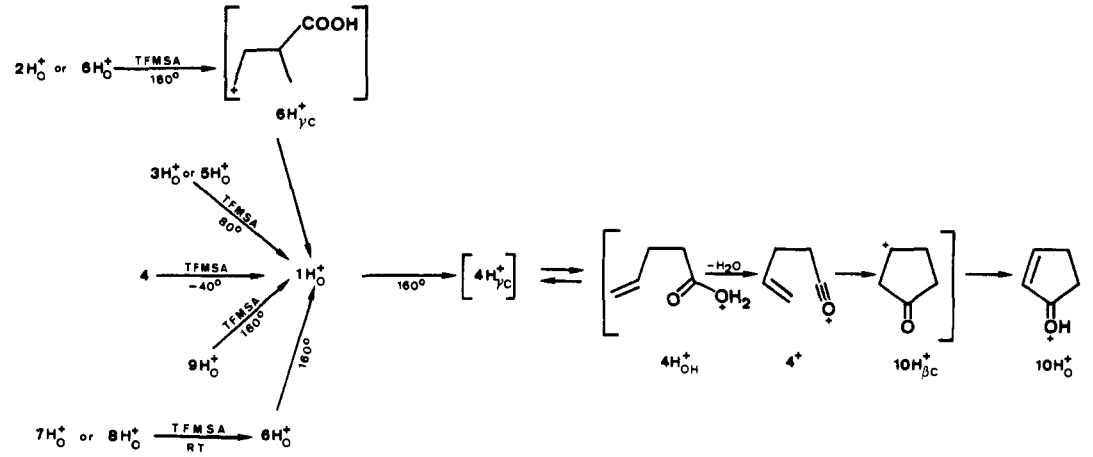
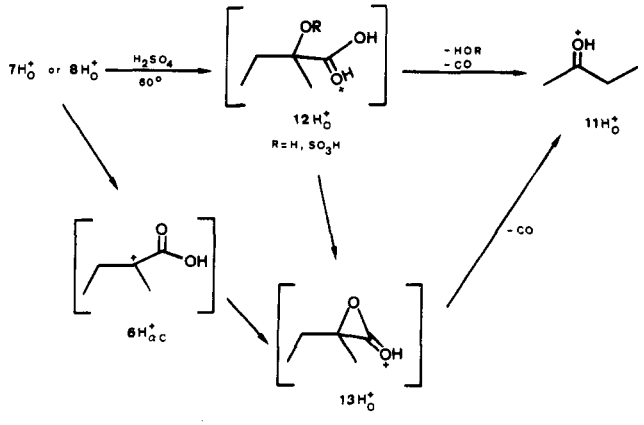
Scheme III



lactones $1H_O^+$ – $3H_O^+$, the carbon atom directly bound to the ether oxygen is also markedly deshielded, which indicates that oxonium ion structures which incorporate an endocyclic carbon–oxygen double bond contribute to the resonance hybrid. The effect is greater here than it is in cations derived from β-lactones, which the contribution by such type of limiting structures is somewhat inhibited due to ring strain.[3] In the protonated unsaturated acids[6] $5H_O^+$ and $6H_O^+$, deshielding of the carbonyl carbon is accompanied by a parallel downfield shift of the signal due to the β-carbon, a result of mesomeric delocalization of the positive charge. The spectra of the protonated cyclopropane carboxylic acids $7H_O^+$ and $8H_O^+$ deserve special comment. In both species, the β-carbons of the cyclopropane ring are unusually deshielded as a result of the protonation of the carbonyl oxygen. This suggests that the charge is delocalized, in part, via the contribution of nonclassical structures similar to those postulated for the cyclopropylmethyl cation.[7] As expected, the ring carbons of protonated cyclobutane carboxylic acid[6] ($9H_O^+$) are deshielded because charge delocalization of the sort found in $7H_O^+$ and $8H_O^+$ is not possible.

Thermally Induced Transformations of the Ions $1H_O^+$–$9H_O^+$. Protonated γ-valerolactone[4] ($1H_O^+$) was stable both in concentrated sulfuric acid and TFMSA even after prolonged (up to 35 h) heating at 80 °C. However, heating $1H_O^+$ at 160 °C in TFMSA solution eventually produced protonated 2-cyclopentenone[8-10] ($10H_O^+$). The presence of that species was detected by ^1H NMR spectroscopy after 45 min of heating. The transformation of $1H_O^+$ to $10H_O^+$ was complete within 9 h. However, when sulfuric acid was the solvent, heating $1H_O^+$ at 160 °C yielded a complex mixture of unidentified sulfonated products. A plausible mechanism for the transformation $1H_O^+ \rightarrow 10H_O^+$ (Scheme III) involves ring opening of $1H_O^+$ to the secondary carbenium ion $4H_{\gamma C}^+$, followed by a reversible C- to O-proton migration, dehydration of the resulting ion $4H_{OH}^+$ to the acylium ion 4^+, cyclization of 4^+ to $10H_{\beta C}^+$, and finally, tautomerization of $10H_{\beta C}^+$ to O-protonated 2-cyclopentenone ($10H_O^+$). Such a mechanism is consistent with the results of recent work on the cyclization of 4^+ to $10H_O^+$.[11]

Scheme IV



The protonated species generated from compounds **3**–**5** and **9**, when heated at 160 °C in TFMSA, gave $10H_O^+$ as the only product. In all four cases, the intermediacy of $1H_O^+$ could be demonstrated by effecting the transformation step-by-step by steadily increasing the reaction temperature from an initially low value. Thus, whereas **4** was quantitatively converted into $1H_O^+$ at –40 °C in TFMSA, the conversion of $3H_O^+$ and $5H_O^+$ required heating at 80 °C for several hours. The cation $9H_O^+$ had to be heated at 160 °C for ring opening to occur. Under such extreme conditions $1H_O^+$ was a minor product, detected only during the early stages of the reaction. The protonated α-methyl derivatives $2H_O^+$ and $6H_O^+$ were stable under prolonged heating at moderate temperatures (60–120 °C) in both sulfuric acid and TFMSA. At 160 °C in the latter solvent both species were converted into $10H_O^+$ via the primary carbenium ion $6H_{\gamma C}^+$.

The thermolysis of the protonated cyclopropanecarboxylic acids $7H_O^+$ and $8H_O^+$ proceeded by two different routes, which were followed depended on the nature of the acidic medium. Thus, in TFMSA at 160 °C quantitative dehydration to yield O-protonated cyclopentenone ($10H_O^+$) occurred. The intermediacy of the ions $6H_O^+$ and $1H_O^+$ was established by monitoring the course of the reaction by ^1H NMR spectroscopy. At temperatures below 60 °C only a clean transformation of $7H_O^+$ and $8H_O^+$ into the unsaturated ion $6H_O^+$ took place. In contrast, in sulfuric acid at such temperatures $7H_O^+$ and $8H_O^+$ lost carbon monoxide to afford O-protonated butanone

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Table II. Relative Intensities (%) of the Peaks in the Chemical Ionization Mass Spectra of the $C_5H_8O_2$ Compounds 1–9[a]

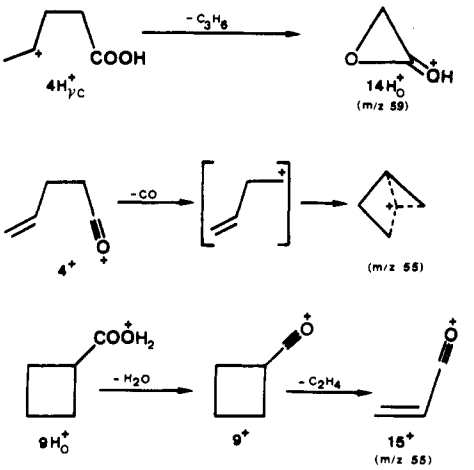
		peak intensity of compd								
m/z	ion	1	2	3	4	5	6	7	8	9
101	$[MH^+]$	100	100	100	75	100	100	100	100	100
100	$[M^{\cdot+}]$			8			18			
99	$[MH^+ - H_2]$				5			12		4
85	$[MH^+ - CH_4]$	2				1		7		
83	$[MH^+ - H_2O]$	22	3	39	100	21	13	24	23	13
82	$[M^{\cdot+} - H_2O]$			3						
81	$[MH^+ - H_2O - H_2]$				4	1				
73	$[MH^+ - CO]/[MH^+ - C_2H_4]$	1	6			1		15	3	4
59	$[MH^+ - C_3H_6]$	5	4	7	25	2		4		2
57	$[MH^+ - C_3H_8]/[MH^+ - CO_2]$	1	7		6	1	4	16	4	
55	$[MH^+ - H_2O - CO]/[MH^+ - H_2O - C_2H_4]$	7	5	12	63	5	4	8	7	14

[a] The reagent gas is methane.

($11H_O^+$). One way this may have happened is depicted in the top part of Scheme IV. Alternatively, $11H_O^+$ could have been formed from $6H_{\alpha C}^+$ via a direct intramolecular nucleophilic attack by the carboxy group oxygen on the cationic center (bottom part of Scheme IV). The latter reaction probably requires a high energy of activation because it is not observed in TFMSA solution.

Transformations of the Ions $1H_O^+$–$9H_O^+$ in the Gas Phase versus Thermally Induced Transformations in Acid Solution. The neutral species 1–9 were submitted to chemical ionization mass spectrometry (CIMS),[12] with methane serving as the reagent gas (see Table II). In all the spectra, an intense $[MH^+]$ ion was observed. The main fragmentation pathway followed by $[MH^+]$ was loss of water to give the ion $[MH^+ - H_2O]$ (m/z 83). This ion might be either an acyl cation or an O-protonated cyclopentenone. It is known that carboxylic acids fragment under the conditions of CIMS to the corresponding acyl cations.[12] The appearance in the spectra of the lactones 1–3 of a peak corresponding to an ion of m/z 83 suggests that all of the initially formed $C_5H_9O_2^+$ ions convert, via ring opening or cyclization or both, to the same species. This observation correlates well with the thermal behavior of the same ionic species in strongly acidic solution. However, only in highly dehydrating solvents like oleum are acyl cations sufficiently stable to be observed spectroscopically.[13] Otherwise, they can be generated at high temperatures, but are only short-lived.[2] Moreover, that, in the spectrum of the acid 4, the base peak (m/z 83) is of a much greater relative intensity than it is in any other case, suggests that cyclodehydration of the ion $[MH^+]$ to yield protonated cyclopentenone ($10H_O^+$) occurs in the gas phase as well as in solution. The presence of the terminal double bond in 4 should facilitate rapid direct intramolecular nucleophilic attack because no prior rearrangement of MH^+ is required. Ions produced by the fragmentation of both C- and O-protonated ions appear in the CIMS spectrum of 4-pentenoic acid (4). The presence of an ion with m/z 59 can be easily rationalized by postulating the loss of propene from the C-protonated species $4H_{\gamma C}^+$. This ion most probably is the protonated α-lactone $14H_O^+$ (Scheme V). Furthermore, the acylium ion 4^+, formed by the dehydration of the O-protonated in $4H_{OH}^+$, would be expected to lose carbon monoxide readily to form the very stable $C_4H_7^+$ ion (m/z 55), one of the most intense peaks in the spectrum (Scheme V). The reason that this ion is so abundant is that it possesses the same framework as the well-known isobaric cyclopropylmethyl and related cat-

Scheme V



ions.[14-17] The peak due to this ion is more intense in the spectrum of 4 than it is in the spectra of the other compounds because it is not necessary for $4H^+$ to rearrange before losing water to form $4H_O^+$, which then loses carbon monoxide. A peak at m/z 55 is also significant in the CIMS spectrum of cyclobutane carboxylic acid (9). However, in this case the peak intensity may reflect a contribution by the isobaric acryloyl cation[3] (15^+), formed via the [2 + 2] cycloreversion of 9^+.

Finally, it is worthy of mention that a relatively intense peak at m/z 73, corresponding to the $[MH - CO]^+$ ion, is observed in the CIMS spectrum of 1-methylcyclopropanecarboxylic acid (7). In view of what is known about the thermochemistry of $7H_O^+$ in acidic solution, it is reasonable to assume that the ion is protonated butanone ($11H_O^+$), formed via loss of carbon monoxide from the protonated α-lactone $13H_O^+$. In this case, it may be that the ions generated during CIMS are energetic enough to overcome the energy barrier associated with a direct nucleophilic attack by the carboxy group oxygen on the carbocationic center of $6H_{\alpha C}^+$.

In summary, with the exception of 4-pentenoic acid (4) the isomeric $C_5H_8O_2$ compounds that were studied underwent O-protonation in strongly acidic solution to afford stable ions which could be characterized by NMR spectroscopy. When heated in solution these ions underwent a series of transformations which eventually yielded pro-

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tonated γ-valerolactone ($1H_O^+$) and, ultimately, O-protonated cyclopentenone ($10H_O^+$) as the most general result. This behavior could be correlated with the behavior of the same ions in the gas phase. Thus, it was possible to assign reasonable structures to the ions that resulted by the fragmentation of the ions initially formed from the parent compounds under the conditions of CIMS.

Experimental Section

^1H NMR spectra were recorded at 60 MHz with a Hitachi Perkin-Elmer Model R-24 NMR spectrometer. ^{13}C NMR spectra were recorded with a Bruker WP 80 SY NMR spectrometer or, when more resolution was necessary, with a Varian Gemini 200 NMR spectrometer. Dioxane or acetone (used for spectra recorded at low temperatures) served as the external standard (capillary tube). Chemical shifts (δ) are reported in ppm relative to TMS. CIMS spectra were recorded with a Hewlett-Packard 5988A spectrometer.

The $C_5H_8O_2$ acids and lactones were commercial materials. Ions were prepared by slowly adding, with efficient stirring, the cooled acid or lactone to a quantity of concentrated sulfuric acid (96%) or neat trifluoromethanesulfonic acid sufficient to give a ca. 1 M solution.

The cationic solutions were heated in tightly closed NMR tubes in a thermostated bath at the temperatures indicated in the text.

^1H NMR Data for the Isomeric $C_5H_9O_2^+$ Ions. $1H_O^+$: 1.6 (d, 3 H), 2.0–2.8 (m, 2 H), 3.3 (t, 2 H), 5.6 (q, 1 H). $2H_O^+$: 1.5 (d, 3 H), 2.6 (m, 2 H), 3.6 (m, 1 H), 5.1 (m, 2 H). $3H_O^+$: 2.0 (bs, 4 H), 3.0 (s, 2 H), 4.9 (s, 2 H). $5H_O^+$: 1.9 (m, 3 H), 2.3 (m, 2 H), 5.9 (d, 1 H), 7.8 (dt, 1 H). $6H_O^+$: 1.9 (s, 3 H), 2.1 (d, 3 H), 7.7 (q, 1 H). $7H_O^+$: 1.2 (s, 3 H), 1.4 (m, 1 H), 1.7 (m, 1 H). $8H_O^+$: 1.2 (d, 3 H), 1.7–1.9 (m, 2 H), 1.9–2.5 (m, 2 H). $9H_O^+$: 1.6–2.6 (m, 6 H), 3.2–3.6 (m, 1 H).

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Registry No. 1, 108-29-2; $1H_O^+$, 140843-82-9; 2, 1679-47-6; $2Ho^+$, 140858-54-4; 3, 542-28-9; $3Ho^+$, 113020-82-9; 4, 591-80-0; 4^+, 94285-35-5; $4Ho^+$, 143430-81-3; 4_{sc}^+, 143430-83-5; 5, 13991-37-2; $5Ho^+$, 115120-39-3; 6, 80-59-1; $6Ho^+$, 143430-77-7; $6H_{ac}^+$, 87676-52-6; $6H_{sc}^+$, 143430-82-4; 7, 6914-76-7; $7Ho^+$, 143430-78-8; 8, 29555-02-0; $8Ho^+$, 143430-79-9; 9, 3721-95-7; $9Ho^+$, 143430-80-2; 9^+, 45377-78-4; $10H_{sc}$, 143446-05-3; $11Ho^+$, 18639-88-8; $12Ho^+$ (R = H), 143430-84-6; $12Ho^+$ (R = SO_3H), 143430-85-7; $13Ho^+$, 143430-86-8; $14Ho^+$, 104598-62-1; 15^+, 35335-83-2; butane ion, 96347-32-9.

Nucleophilic Substitution in 1-Substituted 3-Iodobicyclo[1.1.1]pentanes. A New Synthetic Route to Functionalized Bicyclo[1.1.1]pentane Derivatives

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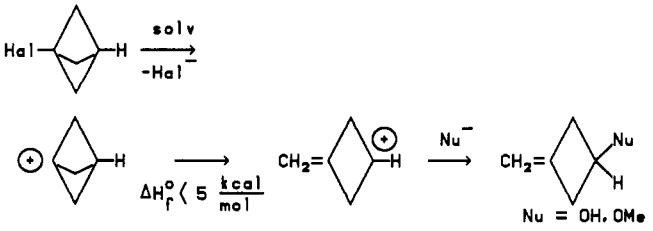
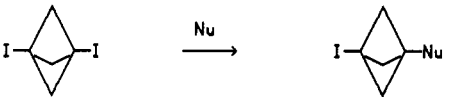
Nucleophilic substitution of the iodine in 1-substituted 3-iodobicyclo[1.1.1]pentanes [R = I (1), CF_3 (2)] was investigated. The results of the reaction are strongly dependent on the nature of the nucleophile and the substituent. Whereas the trifluoromethyl derivative 2 is found to be inert in the reactions and gave substitution products only with organolithium reagents, the 1,3-diiodide 1 is much more reactive and affords normal substitution products with nitrogen bases and MeONa but gives [1.1.1]propellane with Grignard and organolithium reagents and with triaryl(alkyl)phosphines. Other synthesized 3-iodobicyclo[1.1.1]pentanes did not give substitution products. A general scheme for the transformations of 1 is also proposed.

Nucleophilic substitution in cage systems is of great interest in both theoretical and synthetic organic chemistry.[1] However, for the simplest cage molecules such as 1-halobicyclo[1.1.1]pentanes, nucleophilic substitution was believed to be of no practical value,[2] since in 1967 it was discovered that 1-chlorobicyclo[1.1.1]pentane underwent abnormally fast solvolysis with 100% rearrangement.[2a] The same rearrangement was found for other 1-halobicyclo[1.1.1]pentanes.[2b]



It was not until late 1991 that the first successful results for fast unrearranged nucleophilic substitution in 1,3-diiodobicyclo[1.1.1]pentane were reported.[3]



If these reactions are of a general nature, a new effective method for synthesis of 1,3-substituted bicyclo[1.1.1]pentanes is available.

In this paper we present the results of our investigation of these reactions.

Results and Discussion

1,3-Diiodobicyclo[1.1.1]pentane (1) and 1-(trifluoromethyl)-3-iodobicyclo[1.1.1]pentane (2) were chosen as starting materials. Both compounds are very easily prepared in good yield from [1.1.1]propellane in a one-step process.

It was found that 2 has a very low reactivity. Common nucleophiles such as OH^-, MeO^-, RS^-, or R_3N and even

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