# Effects of Solvent and Hydroxyl Deuteration on the Carbon-13 NMR Spectrum of D-Idose: Spectral Assignments, Tautomeric Compositions, and Conformational Equilibria[1]

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Abstract: The ^{13}C NMR spectrum of D-idose with partially deuterated hydroxyls in a Me_2SO/acetone mixture was assigned on the basis of the isotopic multiplets. Then, by tracing the chemical shift curves upon successive dilution, the spectrum in D_2O was also assigned. The percentage of the α- and β-pyranoses and the α- and β-furanoses changes from 38:38:10:14 in the aqueous solution to 26.5:56:10.5:7 in the nonaqueous solvent. Some of the resonances of the α-pyranose form exhibit large upfield shifts, whereas the resonances of the other forms experience small downfield shifts, in going from the aqueous to the nonaqueous solvent. The isotopic multiplets of the α-pyranose show the effects of intramolecular hydrogen bonding equilibria. These observations are interpreted in terms of conformational equilibria involving the α-pyranose form. In going from an aqueous to a nonaqueous solvent, α-D-idopyranose, originally present as a mixture of conformers, assumes almost exclusively the $^4C_1$ conformation, which is stabilized by intramolecular hydrogen bonding interactions.

Reducing sugars, such as the aldohexoses, differ from most other organic compounds in that they exist in solution as a mixture of several species of distinct molecular structure and properties.[2] Idose has a special place among the aldohexose sugars: it has never been crystallized; its aqueous solutions contain substantial amounts of four cyclic tautomers;[3] at least one of the tautomers exists as an equilibrium mixture of conformational isomers;[3,4] its carbon-13 NMR spectrum has remained largely unassigned.[5] Structurally idose is related to glucose: D-idose is epimeric with L-glucose at C-5.

β-D-idopyranose   α-L-glucopyranose
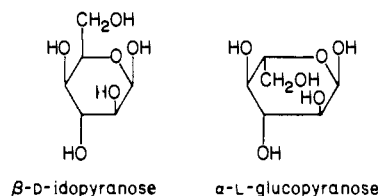
This paper presents results on the tautomeric composition and conformational equilibria of D-idose as obtained from ^{13}C NMR spectra. For assignment purposes the isotopic multiplets in the spectrum of D-idose with partially deuterated hydroxyls (in a Me_2SO/acetone mixture) were examined. The merits of this approach to spectral assignment and structure elucidation of carbohydrates have recently been amply demonstrated.[6–9] The solution was then successively diluted with D_2O and the dilution curves of the chemical shifts of the individual peaks traced.[10] Thus, the spectrum in D_2O was also assigned. In addition, important information was obtained regarding solvent effects on

Tabl I. Tautomeric Composition[a] of D-Idose

form	Me_2SO/acetone	D_2O
α-pyranose	26.5	38
β-pyranose	56	38
α-furanose	10.5	10
β-furanose	7	14

[a] In mole percent ± 1.5.

Table II. Carbon-13 Chemical Shifts[a] of the Tautomers of D-Idose

carbon	solvent	α-p	β-p	α-f	β-f
C-1	Me_2SO/ace.	94.03	91.89	102.10	95.34
	D_2O[b]	93.95	93.20	102.49	96.30
C-2	Me_2SO/ace.	69.39	69.02	81.12	76.09
	D_2O	73.62	70.52	81.61	76.96
C-3	Me_2SO/ace.	69.24	70.41	75.96	75.81
	D_2O	72.68	70.63	75.72	75.86
C-4	Me_2SO/ace.	68.22	67.26	80.14	77.44
	D_2O	71.12	68.72	82.18	78.57
C-5	Me_2SO/ace.	67.49	73.80	69.76	70.20
	D_2O	73.72	75.60	71.75	70.96
C-6	Me_2SO/ace.	59.55	60.11	62.20	61.98
	D_2O	59.38	62.09	63.46	63.34

[a] In ppm using Me_2SO-d_6 as an internal reference at 38.75 ppm. [b] A mixture of 90:5:5 by volume of D_2O, Me_2SO-d_6, and acetone-d_6.

tautomeric composition and conformational equilibria.

Experimental Section

A solution of ca. 0.2 M D-idose in a 1:1 v/v mixture of Me_2SO-d_6 and acetone-d_6 was prepared by taking up 200 mg of the syrupy material (Sigma Chemical Co., St. Louis, Mo.) in 2.5 mL of Me_2SO-d_6 and adding 2.5 mL of acetone-d_6. Partial deuteration was achieved by adding a calculated amount of D_2O. The solution was then treated with molecular sieves and filtered into the NMR tube. Carbon-13 NMR spectra were recorded at 90.56 MHz and 24 ± 1 °C on a Nicolet 360 WB NMR spectrometer operating in the pulsed Fourier transform mode. Low-power broad-band proton decoupling was achieved by using the MLEV-64 pulse sequence.[11] The spectrum of the nonaqueous solution was recorded 5 days after solution preparation. The D_2O dilution experiments were carried out successively during a 24-h period. The spectrum of the solution containing 90% D_2O was acquired during 16 h with a sample that had been in at least 50% D_2O for 12 h and in at least 75% D_2O for 10 h. The central peak of the Me_2SO-d_6 resonance was used as an internal reference. In order to obtain a match with the data of Bock and Pedersen,[5] a chemical shift of 38.75 ppm was assigned to the reference.

(1) Part 6 in the series: "Isotopic Multiplets in the ^{13}C NMR Spectra of Polyols with Partially Deuterated Hydroxyls". For part 5 see: Reuben, J. *J. Am. Chem. Soc.* **1985,** *107,* 1756–1759.

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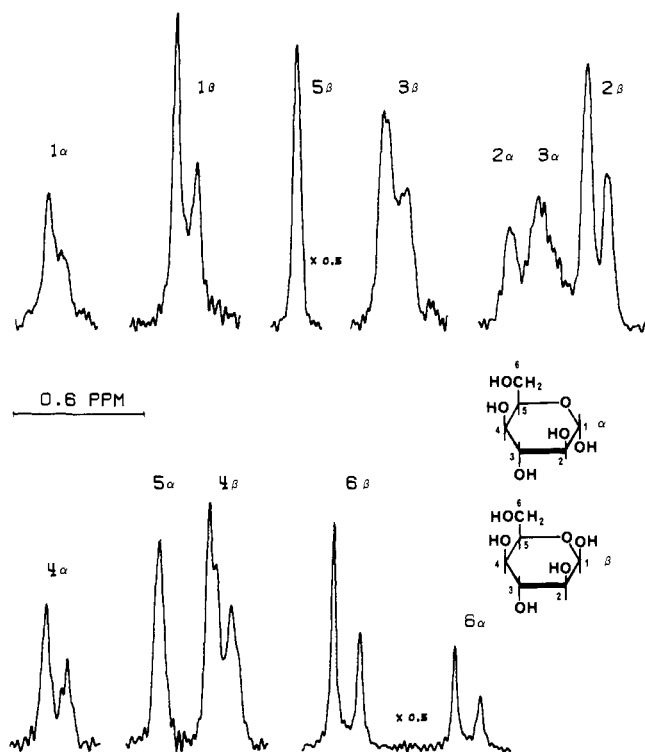
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5868   *J. Am. Chem. Soc., Vol. 107, No. 21, 1985*

Reuben

Figure 1. Isotopic multiplets in the ^{13}C resonances of the D-idopyranoses in a Me_2SO/acetone solution. Chemical shifts are listed in Table II, isotope effects in Table III.
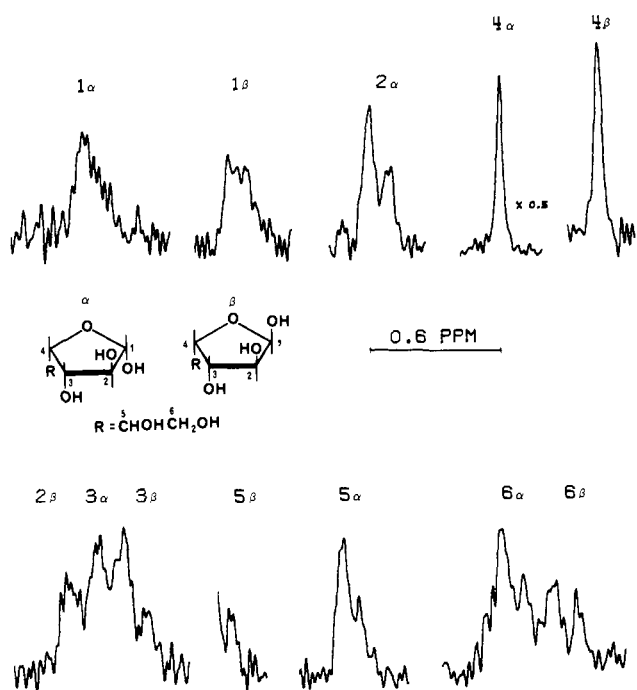

Figure 2. Isotopic multiplets in the ^{13}C resonances of the D-idofuranoses in a Me_2SO/acetone solution. Chemical shifts are listed in Table II.

Results

The ^{13}C NMR spectrum of D-idose in the Me_2SO-d_6/acetone-d_6 mixture contains 24 resonances which can be grouped according to their relative intensities. The four groups thus obtained correspond to four tautomeric forms. The results on the tautomeric composition (as obtained by integration of the signals) are given in Table I. The chemical shift data are summarized in Table II. The spectrum appeared as a set of 12 intense and 12 smaller peaks. The smaller peaks were readily identified with the furanose forms from the resonances in the spectral region above 80 ppm.[5,9] The resonances (exhibiting isotopic multiplets) of the two sets are

Table III. Deuterium Isotope Effects[a] on the ^{13}C Chemical Shifts of the D-Idopyranose Anomers

carbon	α	β
C-1	61, 24	101
C-2	95, 42, 20, 20	97, 19, 19
C-3	100, 48, 26, 26[b]	93, 31, 31
C-4	98, 27, -23[b]	103, 36
C-5	nr[c]	nr[c]
C-6	120	121

[a] Given as δ_H-δ_D in ppb $\pm$ 3.   [b] Obtained by computer simulation. [c] Not resolved.

plotted separately in Figures 1 and 2. The resolution of multiplet structure in these spectra is much lower than observed with other monosaccharides.[6-8] The plausible reason for the line-broadening is the presence in the syrupy idose of trace impurities (e.g., acids or bases) that catalyze hydrogen exchange.

The assignment of the individual resonances relies on well-established structural traits in the chemical shifts of monosaccharides,[5,9] in the patterns of isotopic multiplets, and in the magnitude of isotope effects.[8,9] The chemical shift elements include the low-field position of the anomeric carbons and the high-field position of the methylene carbons, the position at ca. 80 ppm of C-4 of furanoses as well as of C-2 of furanoses with a trans–trans arrangement of hydroxyls (substituents) at carbons 1, 2, and 3, and the C-5 of β-aldopyranoses resonating in the 75–78-ppm region. The deuterium isotope effect for a hydroxylated carbon, Δ_β, is of the order of 100 ppb. The effect from a hydroxyl on a vicinal carbon is smaller: $\Delta_\gamma < 70$ ppb.[6-9] One of the most important structural features of the γ-isotope effect in cyclic vicinal diols is the relationship:[6b]

$$\Delta_\gamma(trans) > \Delta_\gamma(cis) \tag{1}$$

Also, the values of Δ_γ in vicinal diols are not necessarily the same for both carbon atoms. The following inequalities have been observed for monosaccharides:[8]

$$\Delta\gamma(C2,1) > \Delta\gamma(C1,2) \tag{2}$$

$$\Delta\gamma(C3,2) > \Delta\gamma(C2,3) \tag{3}$$

$$\Delta\gamma(C3,4) > \Delta\gamma(C4,3) \tag{4}$$

where C indicates the observed carbon resonance.

Thus (see Figure 1), the α-pyranose was distinguished from the β-pyranose by the γ-isotope effect discernible on the less intense among the anomeric resonances (C-1 of α-p) and by the relatively low-field position of the larger among the two resonances of nonhydroxylated carbons (C-5 of β-p). The resonances of C-6 were assigned on the basis of their position at the high-field end of the spectrum. The least structured of the remaining resonances must be due to C-4, since C-4 has only one hydroxyl on a vicinal carbon. Carbon-2 is distinguished from C-3 on the basis of eq 3 for α-pyranose. Under enhanced resolution the signal of C-2 of β-pyranose appeared, as expected, as a sextet due to a β- and two γ-isotope effects. A summary of the values of the deuterium isotope effects is given in Table III.

The arguments used in assigning the furanose resonances (Figure 2) were similar to those for the pyranoses. Specifically, the resonance at 81.12 ppm exhibits a β-isotope effect and must be due to C-2 of the α-furanose. The resonance next to it (in going upfield) is of similar intensity but lacks splitting and is therefore assigned to C-4 of the α-furanose, whereas the next singlet, which is smaller, is due to C-4 of the β-furanose. In general the furanose resonances have a rather noisy appearance mainly due to the low abundance. Therefore the magnitudes of the isotope effects could not be determined.

A number of conspicuous differences in appearance and magnitude of isotope effects is observed between the resonances of the α- and β-pyranoses (Figure 1). Thus, Δ_β for C-1 of the α-pyranose is much smaller than that of the β-pyranose. The resonance of C-4 of the β-pyranose is a doublet of doublets as expected, whereas C-4 of the α-pyranose is a doublet of (pourly resolved) triplets; i.e., it exhibits structure additional to that ex-
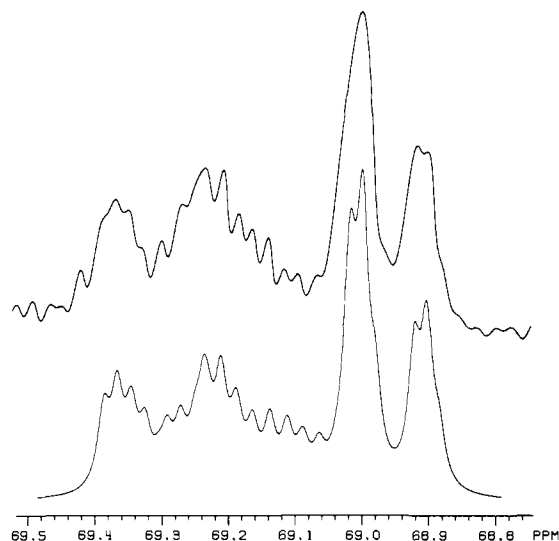
Figure 3. Isotopic multiplets in the resonances of (from left to right) C-2 and C-3 of α-idopyranose and C-2 of β-idopyranose: (top) experimental, (bottom) calculated, with the parameters given in Tables II and III and line widths of 2.2 Hz.

Table IV. Solvent Effects[a] on the ^{13}C Chemical Shifts of the Idose Tautomers

carbon	α-p	β-p	α-f	β-f
C-1	−2.08	−0.69	−1.61	−1.04
C-2	2.23	−0.50	−1.51	−1.13
C-3	1.44	−1.78	−2.24	−1.95
C-4	0.90	−0.54	0.04	−0.87
C-5	4.13	−0.20	−0.01	−1.24
C-6	−2.17	−0.02	−0.74	−1.64

[a] Given as $\delta(D_2O) - \delta(Me_2SO/acetone) - 2.0$, where the last term accounts for the solvent effect on the reference signal.[12]
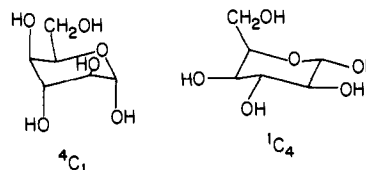
pected according to the simple selection rules.[7,8] Such additional structures is also prominent in the resonances of C-2 and C-3 of the α-pyranose. These resonances along with that of C-2 of the β-pyranose are shown on an expanded scale in Figure 3. The number and magnitude of isotope effects for these resonances were obtained by detailed computer fitting, which took into account the spacing and relative intensities of the multiplet components. The computer simulated spectrum is also shown in Figure 3. The agreement with the experimental spectrum is excellent. It is seen that the low-field components of each multiplet in the experimental spectrum are somewhat broader than the high-field ones. The resolution in the computed spectrum is uniform since it was calculated with the same line width throughout. The high-field components contain a larger proportion of deuterio species for which hydrogen exchange is likely to be slower owing to kinetic isotope effects.

As mentioned, the spectra in aqueous solution were assigned by tracing the dilution curves of the chemical shifts up to a concentration of 90% D_2O. In this way the solvent effects on the chemical shifts were also obtained (see Table IV). A correction of 2 ppm was applied to these results in order to account for the solvent effect on the reference signal.[12] The tautomeric composition (see Table I) was obtained from the relative intensities. The spectrum of D-idose in 90% D_2O is in almost perfect agreement[13] with the chemical shift values given by Bock and Pedersen.[5] These authors give firm assignments only for C-1 and C-6 of the idopyranoses, and C-1, C-2, C-4, and C-6 of the idofuranoses.[5] In the results presented here (see Table II), the assignments of C-1 of the α- and β-pyranoses and of C-2 of the

α-furanose and C-4 of the β-furanose are reversed. The present assignments for the furanoses are in complete accord with those of Angyal[14] obtained on the basis of structural analysis of chemical shifts in monosaccharides. On the other hand, there are major discrepancies in chemical shift values and in assignments with Shashkov's data on the L-idopyranoses.[15] Also, the tautomeric composition of D-idose in 90% D_2O is in good agreement with the results of Angyal and Pickles.[3] Shashkov, on the other hand, did not observe the ^{13}C and ^{1}H NMR signals of the furanose forms but found substantial amounts of 1,6-anhydro-β-L-idopyranose.[15] However, his results[15] on the tautomeric composition of 6-*O*-methyl-L-idose in D_2O are in good agreement with the data for D_2O in Table I.

Discussion

An important phenomenon in solutions of D-idose is the equilibrium between the $^4C_1$ and $^1C_4$ conformations of the α-

pyranose form. Contribution of a skew conformation has also been suggested.[4] The conformational equilibria are rapid on the NMR time scale. From the proton–proton coupling constants Angyal and Pickles[3] estimated the contribution of the $^4C_1$ form in aqueous solution at ca. 1/3. In going from an aqueous to a nonaqueous solvent the conformational equilibria are likely to shift.[16,17] An indication regarding the direction of this change for D-idose can be obtained from the solvent effect on the ^{13}C chemical shifts. Usually in going from D_2O to Me_2SO the ^{13}C resonances of carbohydrates experience downfield shifts.[12] This is indeed the case for the β-pyranose and the α- and β-furanose forms of D-idose (see Table IV). For the α-pyranose, however, the resonances of carbons 2, 3, 4, and 5 experience large upfield shifts. Upfield shifts of such magnitude are usually observed in molecules with axial hydroxyls relative to molecules with equatorial ones.[18] Thus, despite its four axially disposed hydroxyl groups, the $^4C_1$ conformation for the α-D-idopyranose is probably the only one present in the nonaqueous solvent.

In D-idose the α-pyranose and, to a lesser extent, the furanose forms are suppressed in the nonaqueous solvent (see Table I). Usually in nonaqueous solvents the α:β-pyranose ratio is higher than in water and the population of the furanose forms increases.[3,16,19] This phenomenon has been related to the possible integration of the hexopyranose structure into the water structure.[16,19,20] For D-idose, however, the dominant effect on the tautomeric composition seems to be the conformational equilibrium for the α-pyranose. The virtual disappearance of the $^1C_4$ and the skewed conformers in the nonaqueous solvent substantially reduces the entropy of the α-pyranose form leading to its low abundance. A similar shift in conformational equilibrium and in the proportion of the α- and β-pyranoses can be observed in comparing D-idose with D-glycero-D-idoheptose, which has the bulky –CHOHCH$_2$OH substituent on carbon 5.[21] The percentages of the four tautomers for the heptose in D_2O (23, 52, 10, and 15 for the α- and β-pyranoses and the α- and β-furanoses, respectively[21]) are very similar to the ones obtained for D-idose in the nonaqueous solvent (see Table I). As pointed out by Angyal and Tran,[21] in the $^1C_4$ form

(12) Vincendon, M. *Bull. Soc. Chim. Fr.* **1981**, Part II, 129–134.

(13) The only discrepancy involves a listing (under C-5 of α-furanose) of 70.3 ppm. Professor Bock has kindly informed me that this resonance is due to an impurity and that a resonance due to idose is at 71.0 ppm, a value matching the one given in Table II for C-5 of β-furanose.

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of the heptose the extended –CHOHCH$_2$OH side chain has a serious repulsive interaction with the hydroxyl at C-4. As a result this conformer is populated to a lesser extent and the proportion of the α-pyranose in the equilibrium mixture is reduced.

The magnitudes of the deuterium isotope effects (see Table III) on the ^{13}C chemical shifts of β-idopyranose differ only slightly from values observed for a series of other monosaccharides.[8] For α-idopyranose, however, both the magnitudes and the multiplicities are substantially different. Thus, Δ_β for carbon 1 (61 ppb) is much smaller than normally observed (106 ± 9 ppb).[8] Also, carbons 2, 3, and 4 experience long-range isotope effects, beyond the ones expected from the directly bonded hydroxyls and the hydroxyls on vicinal carbons. Similar phenomena observed for α-talopyranose[8] and some β-diols[1] have been interpreted in terms of isotopic perturbations of equilibria involving intramolecular hydrogen bonds. In the $^4C_1$ conformation of α-D-idopyranose the two pairs of syn-diaxial hydroxyls on carbons 1 and 3 and carbons 2 and 4 are ideally situated for intramolecular hydrogen bonding. Indeed the involvement of these hydroxyls in such bonds has been inferred from proton NMR data on idose derivatives.[22,23] One of the equilibria is

$$\text{C4–O4–H}\cdots\text{O2–H} \rightarrow \text{C2–O2–H}\cdots\text{O4–H} \qquad (5)$$
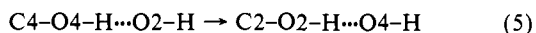
Deuteration of either O4–H or O2–H is likely to perturb this equilibrium with the results sensed by carbons 2 and 4, respectively. The situation is similar to the one described in detail for α-talopyranose.[8] Hydroxyls attached to anomeric carbons seem to participate in hydrogen bonds almost exclusively as the hydrogen donors.[24] Therefore, for the hydroxyls on carbons 1 and 3 an equilibrium involving structures with and without the C1–O1–H$\cdots$O3–H hydrogen bond is suggested. Isotopic perturbation of this equilibrium upon deuteration of the anomeric hydroxyl results in the additional isotope effect on the chemical shift of carbon 3 and in modification of the intrinsic isotope effect on the chemical shift of carbon 1. The chemical shift manifestation of isotopic

perturbation on an equilibrium is more probable when the equilibrium constant is close to unity.[8] The absence of extra splittings in the isotopic multiplets of β-idopyranose, where an equilibrium involving the hydroxyls on carbons 2 and 4 (eq 5) is also possible, indicates that one of the structures in the equilibrium is strongly favored.

For α-D-idopyranose, the preponderance of intramolecular hydrogen bonding interactions in the nonaqueous solvent[17] is probably one of the main factors responsible for the shift toward the $^4C_1$ conformation, in which such interactions are possible. Moreover, the accessibility of several states with intramolecular hydrogen bonds (as the isotopic multiplets have demonstrated) leads to further stabilization of this conformation. However, these relatively weak interactions should have little direct effect on the tautomeric equilibrium, which proceeds on an energy scale corresponding to the breaking and formation of covalent bonds. Entropic considerations suggest that the conformational equilibrium is affected by the number of states available to each conformer, whereas the tautomeric equilibrium is affected by the number of conformers for each species.

Conclusions

The solvent dependence of the tautomeric composition and ^{13}C chemical shifts of D-idose as well as the deuterium isotope effects and the isotopic multiplets all lead to the following simple picture. In going from an aqueous to a nonaqueous solvent, α-D-idopyranose, originally present as a mixture of conformers, assumes almost exclusively the $^4C_1$ conformation, which is stabilized by intramolecular hydrogen bonding interactions. The conformational equilibrium of the α-pyranose form appears to be the key phenomenon in solutions of D-idose.

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Transition-Metal–Carbene Chemistry. Structure, Thermodynamics, and Reactivity of RhCH$_2^+$ in the Gas Phase

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Abstract: The first studies involving a second-row transition-metal methylidene ion, RhCH$_2^+$, in the gas phase using Fourier transform mass spectrometry (FTMS) are described. Product distributions for the reactions of RhCH$_2^+$ with hydrogen, methane, ethane, ethene, propene, and cyclopropane are reported. The methylene bond strength, $D°(\text{Rh}^+\text{–CH}_2)$, was bracketed between 92 and 95 kcal/mol from which $D°(\text{Rh}^+\text{–CH}_2) = 94 \pm 5$ kcal/mol is assigned. Structural studies clearly indicate formation of a methylidene–rhodium complex instead of a hydrido–methylidyne species. Collisional activation of RhCH$_2^+$ yields both RhC$^+$ and Rh$^+$, suggesting that α-hydride abstraction in RhCH$_2^+$ can occur. RhCH$_2^+$ reacts readily with both hydrogen and methane and represents the first example of methane activation by a cationic mononuclear transition-metal complex in the gas phase. The activation energy for methane elimination from Rh(H)(CH$_3$)$^+$ appears to be less than 5 kcal/mol. α-Hydride abstraction from Rh(CH$_3$)$_2^+$ resulting in methane elimination is found to be facile. Reactions of Rh$^+$ with cyclopropane and RhCH$_2^+$ with ethene suggest that β-hydride elimination from a rhodacyclobutane intermediate occurs readily. Therefore, the rhodacyclobutane$^+$ ring is believed to have significant puckering. Finally, metathesis products are observed for reactions of RhCD$_2^+$ with both ethene and propene. The results of this work are compared to earlier studies on first-row MCH$_2^+$ ions.

Transition metal–carbenes[1,2] have been implicated as intermediates in a variety of important catalytic transformations including olefin metathesis,[3–7] the Ziegler-Natta polymerization of olefins,[8,9] cyclopropane formation from olefins,[10,11] olefin homologation,[12] metal–alkyl decompositions,[13–15] and the heterogeneous Fischer–Tropsch process.[16] Despite the important role