# The Negative Ion Mass Spectra of Deprotonated Carbohydrates. Part 1. The Basic Hydroxymethyl-substituted Ring Systems

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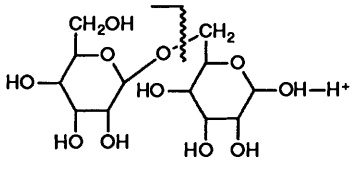
Tetrahydrofuran-2-methanol and tetrahydropyran-2-methanol are models for the basic ring systems of simple carbohydrates. These compounds deprotonate, in the gas phase, principally at the HO group. The major fragmentations of these systems involve competitive losses of $H_2O$ and $CH_2O$. Labelling ($^{18}O$ and $^{2}H$), and product ion studies, indicate that proton transfer between the 3-position on the ring and $-CH_2O^-$ yields a 3-anion which immediately ring opens. The ring opened alkoxide may undergo proton transfers which effectively make both of the oxygens equivalent. Other tetrahydrofuran- and tetrahydropyran-methanols also undergo ring cleavage: their negative ion spectra show subtle differences.

There has been a plethora of reports concerning the use of negative ion mass spectrometry, particularly fast atom bombardment, to assist in the structure determination of underivatised carbohydrate containing compounds (for reviews, see ref. 1). The negative ion technique has been primarily used to provide molecular weight information,[1] but sequence information, involving carbon–oxygen bond cleavage of the glycosidic linkages, is also available.[1–4] Cleavage of individual ring systems has also been reported.[5–7] In particular, extensive fragmentation of some deprotonated disaccharides has been described.[7] For example, ions of type **1** undergo the simple cleavage indicated, but also lose $H_2O$, $CH_2O$, $C_2H_4O_2$ and $C_3H_6O_3$. The mechanisms of these reactions are not fully understood.

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The determination of the mechanisms of such complex ring cleavages will be aided by an understanding of the fragmentation behaviour of the 'parent' carbohydrate ring systems. Thus, this paper describes the collision-induced dissociations of the deprotonated forms of (i) tetrahydrofuran and tetrahydropyran, and (ii) all of the monohydroxymethyl derivatives of these two ring systems. The fragmentations are complex; their elucidation required extensive labelling ($^{2}H$ and $^{18}O$) and product ion studies.

## Results and Discussion

(a) *The Parent Ring Systems.*—In the condensed phase, both tetrahydrofuran and tetrahydropyran react with strong base at the 2-position. For example, (i) both compounds react with butylpotassium to form the 2-potassium salt, presumably

**Table 1** Collision induced dissociations of ions derived from tetrahydrofuran, tetrahydropyran and related species

| Ion ($m/z$) | | Spectrum type [CA—collisional activation CR—charge reversal (positive ion)] | Spectrum [$m/z$ (loss) abundance] for CA $m/z$ (abundance) for CR |
|---|---|---|---|
|  $-H^+$ | (71) | CA MS/MS<br>CR MS/MS | 69 ($H_2$) 15, 41 ($CH_2O$) 100,[a] 17 ($C_4H_6$) 2<br>41 (31), 39 (100), 38 (28), 29 (49), 27 (33), 26 (27), 15 (8), 14 (6), 13 (5) |
| $CH_2{=}CH(CH_2)_2O^-$ | (71) | CA MS/MS<br>CR MS/MS | 69 ($H_2$) 14, 41 ($CH_2O$) 100,[b] 17 ($C_4H_6$) 2<br>41 (37), 39 (100), 38 (23), 29 (43), 27 (29), 26 (25), 15 (7), 14 (5), 13 (3) |
|  $-H^+$ | (85) | CA MS/MS<br>CR MS/MS | 83 ($H_2$) 6, 67 ($H_2O$) 9, 55 ($CH_2O$) 100[c]<br>55 (15), 53 (14), 51 (18), 41 (28), 39 (100), 29 (57), 28 (27), 27 (55), 15 (3), 14 (2) |
| $CH_2{=}CH(CH_2)_3O^-$ | (85) | CA MS/MS<br>CR MS/MS | 83 ($H_2$) 7, 67 ($H_2O$) 8, 55 ($CH_2O$) 100[d]<br>55 (12), 53 (12), 51 (16), 41 (25), 39 (100), 29 (59), 28 (26), 27 (54), 15 (2), 14 (2) |
|  $-H^+-CH_2O$ | (55) | CA MS/MS/MS<br>CR MS/MS/MS | 54 (H) 100, 53 ($H_2$) 44, 27 ($C_2H_4$) < 5[e]<br>55 (85), 54 (53), 53 (54), 52 (26), 51 (31), 50 (28), 49 (12), 41 (8), 40 (10), 39 (100), 38 (17), 37 (28), 29 (43), 28 (21), 27 (71), 26 (48), 15 (5) |
| $CH_2{=}CH(CH_2)_3O^-$ $-CH_2O$ | (55) | CA MS/MS/MS<br>CR MS/MS/MS | 54 ($H^\cdot$) 100, 53 ($H_2$) 46, 27 ($C_2H_4$) < 5[e]<br>55 (82), 54 (54), 53 (52), 52 (28), 51 (30), 50 (26), 49 (10), 41 (8), 40 (11), 39 (100), 38 (18), 37 (29), 29 (41), 28 (20), 27 (70), 26 (47), 15 (4) |

Peak widths at half height [a] 23.3 ± 0.2 V. [b] 23.1 ± 0.2 V. [c] 32.0 ± 0.3 V. [d] 31.8 ± 0.3 V. [e] Weak spectrum, difficult to quantify because of baseline noise.

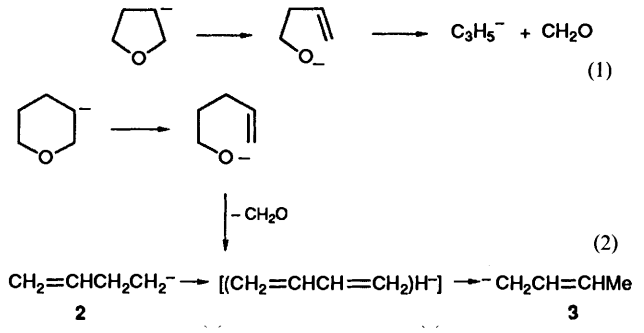
**Table 2** Collisional activation mass spectra of hydroxymethyltetrahydrofurans and tetrahydropyrans and certain deuterium labelled derivatives (THF = tetrahydrofuran: THP = tetrahydropyran)

| | Loss | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Parent ion | H$^{\cdot}$ | D$^{\cdot}$ | $H_2$ | HD | $H_2O$ | HOD | $CH_2O$ | $CD_2O$ | $2H_2O$ | ($H_2O$ + HOD) | ($H_2O$ + $CH_2O$) | (HOD + $CH_2O$) | ($H_2O$ + $CD_2O$) | (HOD + $CD_2O$) | $2CH_2O$ | ($CH_2O$ + $CD_2O$) | $C_3H_6$ | $C_3H_5D$ |
| THF-2-$CH_2OH$ – $H^+$ | 4 | | 8 | | 79 | | 100 | | | | 3 | | | | | | 6 | |
| THF-2-$CD_2OH$ – $H^+$ | 3 | 2[a] | 2[a] | 1 | 100 | | 43 | 13 | | | 2 | | | | | | 4 | |
| THF-2-$CD_2OD$ – $D^+$[b] | 3 | 2[a] | 2[a] | 1 | 100 | | 45 | 12 | | | 2 | | 0.3 | | | | 4 | |
| THF-2-$CD_2OD$ – $H^+$[b] | 4 | 2[a] | 2[a] | 1 | 100 | 48 | 64 | 21 | | | 1 | 0.5 | 0.1 | | | | | 5 |
| THF-2-D-2-$CH_2OH$ – $H^+$ | 1 | 2[a] | 2[a] | 1 | 100 | 6 | 92 | | | | 2 | | | | | | 4 | |
| THF-3-$CH_2OH$ – $H^+$ | 8 | | 6 | | 100 | | 54 | | | | | | | | | | | |
| THF-3-$CD_2OH$ – $H^+$ | 8 | | | 5 | 100 | | 54 | 46 | | | | | | | | | | |
| THF-3-$CD_2OD$ – $D^+$[c] | 8 | | | 5 | 100 | | 53 | 45 | | | | | | | | | | |
| THF-3-$CD_2OD$ – $H^+$[c] | 6 | 3[a] | 3[a] | 4 | 100 | 52 | 71 | 58 | | | | | | | | | | |
| THP-2-$CH_2OH$ – $H^+$ | 5 | | | | 100 | | 8 | | 2 | | 41 | | | | | | | |
| THP-2-$CD_2OH$ – $H^+$ | 6[d] | | 6[d] | | | 100 | | 5 | 5 | 2 | | 51 | | 10 | | | | |
| THP-2-$CD_2OD$ – $D^+$[e] | 5[d] | | 5[d] | | | 100 | | 5 | 5 | 2 | | 50 | | 10 | | | | |
| THP-2-$CD_2OD$ – $H^+$[e] | 8[d] | | 8[d] | | 1 | 100 | 54 | 10 | 8 | 5 | 2 | 41 | 20 | 8 | | 8 | | |
| THP-3-$CH_2OH$ – $H^+$ | | | 56 | | 9 | | 100[f] | | | | 28 | | | | | 27 | | |
| THP-3-$CD_2OH$ – $H^+$ | | | | 20 | 13 | | 27 | 100 | | | 24 | | | 23 | | | 34 | |
| THP-3-$CD_2OD$ – $D^+$[g] | | | | | 15 | | 29 | 100 | | | 22 | | | 21 | | | 36 | |
| THP-3-$CD_2OD$ – $H^+$[g] | | | | 28 | 19 | 10 | 32 | 100 | | | 20 | 8 | | 19 | 4 | | 32 | |
| THP-4-$CH_2OH$ – $H^+$ | | | 4 | | 100 | | 8 | | | | 4 | | | | | 2 | | |
| THP-4-$CD_2OH$ – $H^+$ | | | | 3 | 100 | | 1 | 6 | | | 3 | | | 1 | | | 1 | |
| THP-4-$CD_2OD$ – $D^+$[h] | | | | 2 | 100 | | 1 | 6 | | | 3 | | | 1 | | | 1 | |
| THP-4-$CD_2OD$ – $H^+$[h,j] | | | | | 100 | 17 | | 9 | | | | | | | | | | |

| | Formation | | | | | | |
|---|---|---|---|---|---|---|---|
| Parent ion | $HOCH_2O^-$ | $DOCH_2O^-$ | $HOCD_2O^-$ | $DOCD_2O^-$ | $HC_2O^-$ | $HO^-$ | $DO^-$ |
| THF-2-$CH_2OH$ – $H^+$ | 11 | | | | | 8 | |
| THF-2-$CD_2OH$ – $H^+$ | 3 | | 5 | | | 3 | |
| THF-2-$CD_2OD$ – $D^+$[b] | 3 | | 5 | | | 4 | |
| THF-2-$CD_2OD$ – $H^+$[b] | 2.5 | 1 | 2 | 0.5 | | 3 | 1 |
| THF-2-D-2-$CH_2OH$ – $H^+$ | 12 | | | | | 6 | |
| THF-3-$CH_2OH$ – $H^+$ | 15 | | | | 8 | 1 | |
| THF-3-$CD_2OH$ – $H^+$ | 6 | | 4.5 | | 3 | 1 | |
| THF-3-$CD_2OD$ – $D^+$[c] | 6 | | 5 | | 3 | 1 | |
| THF-3-$CD_2OD$ – $H^+$[c] | 3 | 1 | 3 | 1 | 2 | 1 | 0.5 |
| THP-2-$CH_2OH$ – $H^+$ | | | | | | | |
| THP-2-$CD_2OH$ – $H^+$ | | | | | | | |
| THP-2-$CD_2OD$ – $D^+$[e] | | | | | | | |
| THP-2-$CD_2OD$ – $H^+$[e] | | | | | | | |
| THP-3-$CH_2OH$ – $H^+$ | 7 | | | | | | |
| THP-3-$CD_2OH$ – $H^+$ | 6 | | 6 | | | | |
| THP-3-$CD_2OD$ – $D^+$[g] | 6 | | 6 | | | | |
| THP-3-$CD_2OD$ – $H^+$[g] | 4 | 5 | 2 | 4 | | | |
| THP-4-$CH_2OH$ – $H^+$ | | | | | | | |
| THP-4-$CD_2OH$ – $H^+$ | | | | | | | |
| THP-4-$CD_2OD$ – $D^+$[h] | | | | | | | |
| THP-4-$CD_2OD$ – $H^+$[h,j] | | | | | | | |

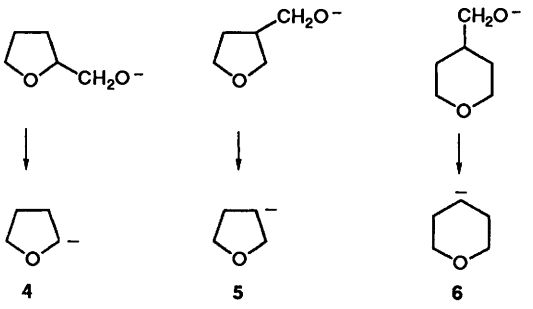
[a] D$^{\cdot}$ = $H_2$ = 2 a.m.u. [b] $-D^+ : -H^+ = 9:1$. [c] $-D^+ : -H^+ = 8.5:1$. [d] Unresolved. [e] $-D^+ : -H^+ = 9:1$. [f] This spectrum also shows a peak formed by loss of ($H_2$ + $CH_2O$) 15%. [g] $-D^+ : -H^+ = 10:1$. [h] $-D^+ : -H^+ = 15:1$. [j] Weak spectrum—peaks of less than 5% abundance lost in background noise.

following association of the organometallic reagent at oxygen,[8] and (ii) tetrahydrofuran reacts with butyllithium to yield the 2-lithium salt which decomposes to form ethylene and acetaldehyde.[9] A very different scenario is apparent in the gas phase. DePuy, using flowing afterglow experiments, has shown that both tetrahydrofuran and tetrahydropyran are deprotonated exclusively at the 3-position by strong bases, followed by an E2 reaction to form the ring-opened alkoxide ion.[10] For example, deprotonation of tetrahydrofuran by $HO^-$ or $NH_2^-$ yields the alkoxide ion derived from but-3-en-1-ol.




These observations are in accord with the data shown in Table 1. The collisional activation (CA) and charge reversal (CR)[11] mass spectra (MS/MS) of deprotonated tetrahydrofuran and tetrahydropyran indicate that the decomposing species correspond to the alkoxide ions of but-3-en-1-ol [eqn. (1)] and pent-4-en-1-ol [eqn. (2)], respectively. The major negative ion fragmentation shown in eqn. (1) is the standard[12] loss of formaldehyde to yield the allyl anion. Loss of formaldehyde is also the major loss in the tetrahydropyran system [eqn. (2)], except that in this case, the first formed product ion is likely to be the unstable β-vinylethyl anion **2**, which is known[13,14] to rearrange to the stable but-2-ene ion **3** [the MS/MS/MS data recorded in Table 1 identify the product ion $C_4H_7^-$ as **3** (*cf.* ref. 14)]. Other fragmentations of the alkoxide ion of pent-4-en-1-ol include the losses of $H_2$ and $H_2O$: these are standard reactions of an alkoxide system.[15]

(b) *The Hydroxymethyl-substituted Ring Systems.*—Although the 2-methanol derivatives of tetrhydrofuran and tetrahydropyran are the carbohydrate model systems, we have studied all of the five monohydroxymethyl derivatives for the following reason. These compounds should deprotonate preferentially at the hydroxy group (substantiated experimentally, see later), and such compounds could, in principle, undergo the standard loss of formaldehyde to form, for example, the interesting anions **4**–**6** (Scheme 1). If this were so, then **4** should decompose to ethylene and deprotonated acetaldehyde (as noted in the condensed phase[9]), whereas **5** should ring open in the manner shown in eqn. (1). However, it is possible that ions like **4** and **6** will be either short-lived or unstable, because the electron affinities of the corresponding radicals may be close to zero or even negative [*cf.* $E_a$ ($MeOCH_2^{\cdot}$), −39 kJ $mol^{-1}$[16]].* Given such a circumstance, unusual fragmentations may be observed, perhaps following specific proton transfer to the initial deprotonated site (for a review of negative ion cleavages, see ref. 18).




**Scheme 1**

The spectra (MS/MS) of the deprotonated tetrahydrofuran and tetrahydropyran-methanols together with those of various deuteriated derivatives are shown in Table 2, while those of $^{18}O$ labelled derivatives are illustrated in Figs. 1 and 2. Fragmentation data (MS/MS/MS) of selected product ions are listed in Table 3.

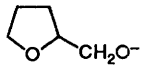
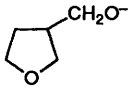
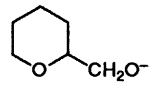
The spectra (Table 2) of the unlabelled compounds look deceptively simple; the major processes involve competitive losses of $H_2O$ and $CH_2O$. However, even a cursory look at the spectra of the deuteriated (Table 2) and $^{18}O$ labelled derivatives (Figs. 1 and 2) indicate the spectra to be complex. For example, all spectra shown in Figs. 1 and 2 show peaks corresponding to losses of $H_2O$, $H_2{}^{18}O$, $CH_2O$ and $CH_2{}^{18}O$.

The initial clue to the nature of the fragmentations is given by the sites of deprotonation of these systems. Consider the case of tetrahydrofuran-2-methanol since this is typical of and analogous to the behaviour of all other compounds studied. The following observations follow from the data contained in Table 2. (i) Deprotonation occurs principally at the HO group, but there is minor deprotonation at the 3-position(s) on the ring. For example, THF-2-$CD_2OD$ when allowed to react with $DO^-$, yields ($M - D^+$) and ($M - H^+$) in the ratio 9:1, where both THF-2-D-2-$CH_2OH$ and THF-2-$CD_2OH$ give only ($M - H^+$) ions with $HO^-$. (ii) The mass spectra of (THF-2-$CD_2OH$ − $H^+$) and (THF-2-$CD_2OD$ − $D^+$) are identical. (iii) The fragmentations noted in the spectra of the ($M - D^+$) and ($M - H^+$) ions from THF-2-$CD_2OD$ are the same in general terms. There are, of course, differences in detail: for example, the former specifically loses $H_2O$, while the latter loses both $H_2O$ and HOD. It can be concluded from these observations that since the alkoxide and the (decomposing) 3-carbanion fragment in the same manner, then either one ion is convertible into the other following collisional activation (*e.g.* **7** ⟶ **8**, Scheme 2) or perhaps both are in equilibrium.

The labelling and product ion studies are in accord with the following proposals. Proton transfer **7** ⟶ **8** followed by ring opening forms the alkoxide **9**. Since Fig. 1 shows almost equal losses of $H_2O$ and $H_2{}^{18}O$ (there is an $^{18}O$ isotope effect $^{16}O/^{18}O$ = 1.15, see later), it is likely that both oxygen atoms are equivalent in the decomposing species. This can be accomplished by equilibration **9** ⇌ **10** (which requires two proton transfers between oxygens, and two proton transfers between oxygen and allylic methylene positions). Fragmentation of **9** and **10** (one shown) produces $HO^-$ [eqn. (3)] together with elimination of $H_2O$ [eqn. (4)]. The loss of water shows the following isotope effects: $^{16}O/^{18}O$ = 1.15 (see Fig. 1), and H/D = 2.08 [see the spectrum of (THF-2-$CD_2OD$ − $H^+$) (Table 2)]. This is consistent with either a concerted process, or, more likely, one in which both steps are kinetically significant (*cf.* ref. 19).

* Further circumstantial evidence indicating the relative stabilities of ions like **4**–**6** is given by the following experiments. Another standard method for making $R^-$ ions in the gas phase involves decarboxylation of carboxylates $RCO_2^-$.[12,17] The tetrahydrofuran and tetrahydropyran carboxylic acids were all available in this study, so the collision induced decompositions of their carboxylate ions were investigated. As expected, the two 3-carboxylate ions show moderate loss of $CO_2$ [*cf.* eqns. (1) and (2)], while the two 2-carboxylate ions show no peaks associated with loss of $CO_2$. Interestingly, the 4-carboxylate ion of tetrahydropyran does exhibit minor loss of $CO_2$—perhaps **6**, or some rearranged form is stable.

**Table 3** MS/MS/MS data for deprotonated hydroxymethyl derivatives

| Precursor ion (*m/z*) | Product ion (*m/z*) | Spectrum type | Spectrum CA [*m/z* (loss) abundance] CR [*m/z* (abundance)] |
|---|---|---|---|
|  (101) | $-H_2O$ (83) | CA[a] | 81 ($H_2$) 100, 65 ($H_2O$) < 10, 53 ($CH_2O$) 50 |
| | | CR | 82 (26), 81 (44), 66 (12), 65 (8), 53 (85), 51 (54), 41 (12), 39 (100), 29 (38), 27 (83), 15 (5) |
| | $-CH_2O$ (71) | CA[a] | 69 ($H_2$) 100, 53 ($H_2O$) 95, 37 ($C_2H_4O$) 20 |
| | | CR | 70 (18), 69 (42), 55 (14), 54 (58), 53 (41), 51 (23), 43 (31), 41 (36), 39 (100), 31 (40), 29 (31), 27 (43), 15 (5), 14 (3) |
| | $-C_3H_6$ (59) | CR | 59 (18), 42 (28), 41 (8), 29 (100), 15 (18), 14 (17) |
| | $-CH_4O_2$ (53) | CR | 53 (56), 52 (45), 51 (100), 50 (35), 39 (16), 38 (46), 27 (72), 26 (14) |
| | $-C_4H_6$ (47) | CR | 45 (36), 30 (54), 29 (100) |
|  | $-H_2O$ (83) | CA[a] | 81 ($H_2$) 35, 53 ($CH_2O$) 100 |
| | | CR | 82 (48), 81 (42), 66 (10), 53 (68), 51 (45), 41 (18), 39 (100), 29 (58), 27 (57), 15 (8) |
| | $-CH_2O$ (71) | CA[a] | 69 ($H_2$) 25, 53 ($H_2$) 100 |
| | | CR | 70 (14), 69 (24), 54 (38), 53 (37), 51 (22), 43 (27), 41 (38), 39 (100), 31 (28), 29 (24), 27 (53), 15 (9), 14 (6) |
|  | $-H_2O$ (97) | CA | 79 ($H_2O$) 16, 67 ($CH_2O$) 100 |
| | | CR | 95 (12), 81 (12), 79 (21), 77 (14), 67 (100), 65 (46), 63 (16), 53 (40), 51 (40), 42 (63), 39 (95), 31 (18), 29 (16), 27 (50), 15 (6) |
| | $-CH_2O$ | (85)CA[a] | 67 ($H_2O$) 50, 55 ($CH_2O$) 100 |
| | | CR | 67 (31), 65 (15), 55 (76), 53 (68), 51 (28), 41 (61), 39 (100), 29 (73), 27 (76), 15 (5) |
| | $-CH_4O_2$ (67) | CR | 67 (100), 66 (94), 65 (76), 63 (16), 53 (16), 52 (20), 51 (31), 50 (22), 41 (58), 40 (40), 39 (98), 27 (41), 25 (12). |

[a] Collisional activation spectrum is weak—time average of 100 scans.

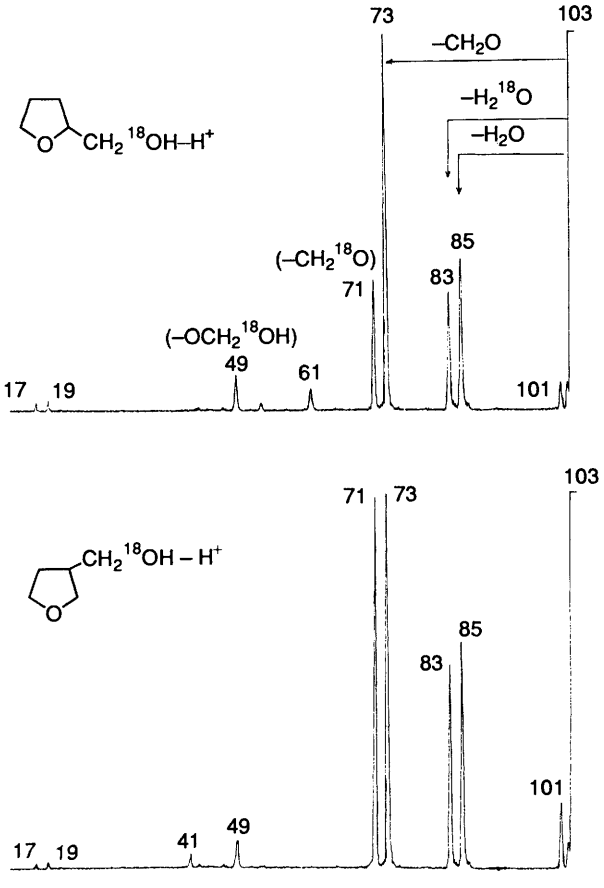
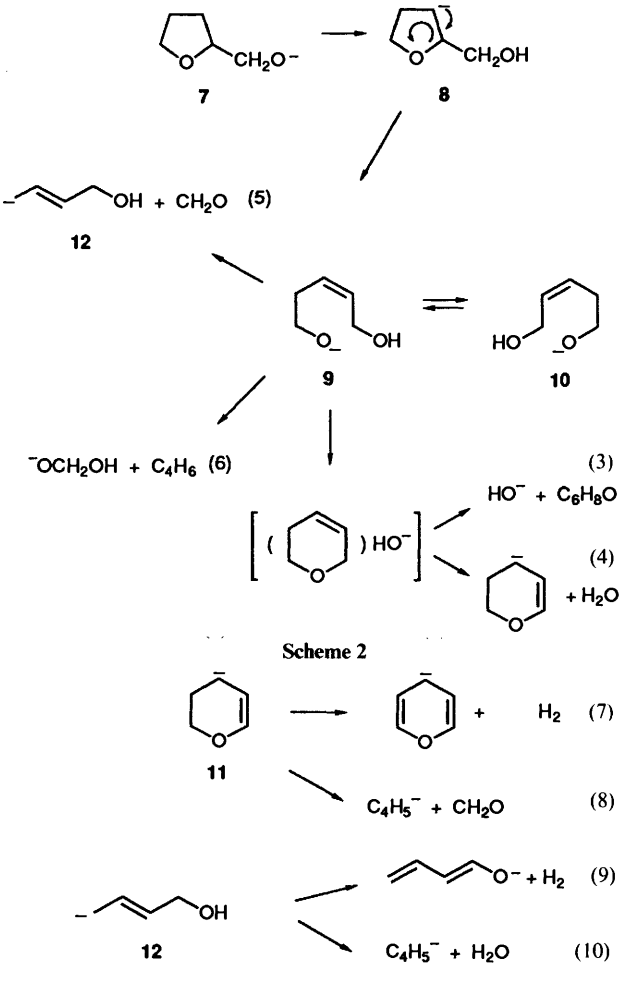



Fig. 1




Scheme 2

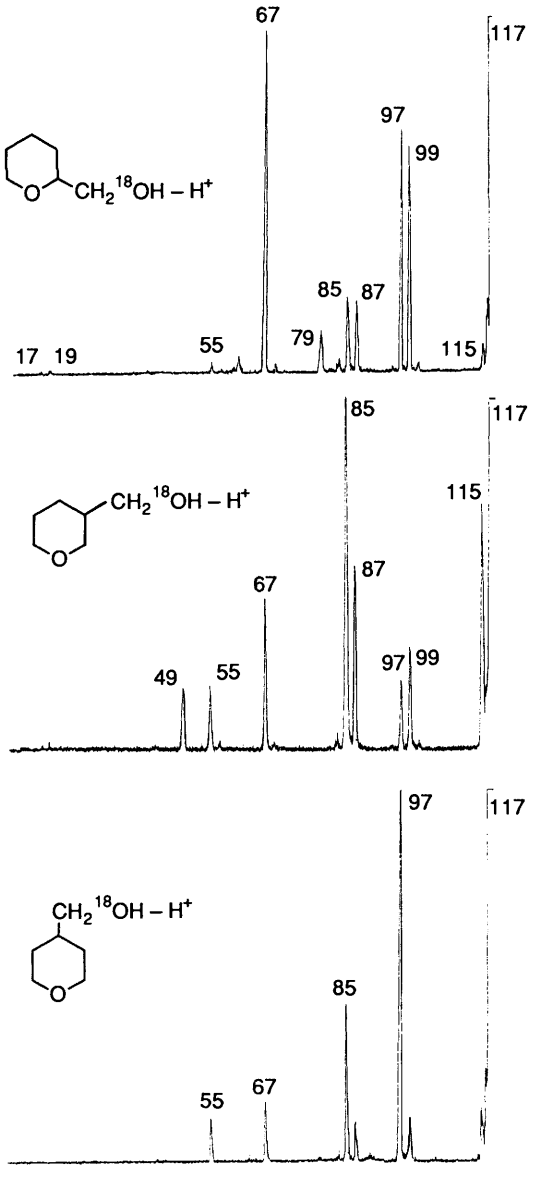
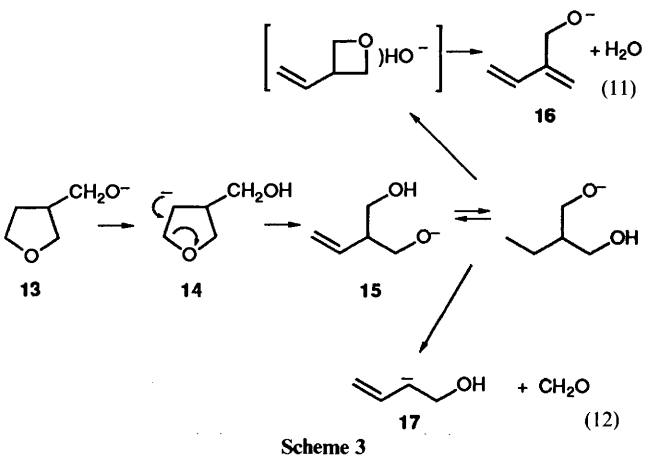


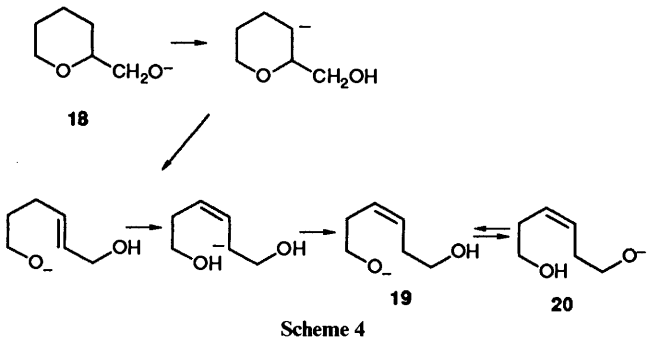

Fig. 2

The loss of $CH_2O$ is clearly a faster process than loss of $H_2O$ since fragmentation proceeds mainly *via* **9** [eqn. (5)] rather than **10** [*i.e.* (THF-2-$CD_2OH$ – $H^+$) loses $CH_2O$:$CD_2O \simeq 3:1$ (Table 2), while (THF-2-$CH_2{}^{18}OH$ – $H^+$) loses $CH_2O$:$CH_2{}^{18}O \simeq 2.5:1$ (Fig. 1)]. The formation of $HOCH_2O^-$ [eqn. (6)] also proceeds mainly through **9** [*i.e.* (THF-2-$CD_2OH$ – $H^+$) forms $HOCD_2O^-$:$HOCH_2O^- = 2.5:1$]. The structures proposed for the major product ions **11** and **12** are in accord with their fragmentation data (Table 3). For example, the negative ion cleavages of **11** involve the losses of $H_2$ [eqn. (7)] and $CH_2O$ [eqn. (8)], whereas **12** loses $H_2$ [eqn. (9)] and $H_2O$ [eqn. (10)].

The behaviour of deprotonated tetrahydrofuran-3-methanol is very similar to that of the 2-isomer, except that in this case, the loss of $CH_2O$ involves both oxygens equally (Table 2 and Fig. 1). The rationale shown in Scheme 3 is in accord with labelling and product ion studies. Proton transfer **13** ⟶ **14**, followed by ring cleavage yields **15**. Here, equilibration of the two oxygens requires only proton transfer between the two oxygens. Loss of water [eqn. (11)] yields **16**; this process shows $^{16}O/^{18}O$ (1.16, Fig. 1) and $^1H/^2H$ (1.92, Table 2) isotope effects. The fragmentation data (Table 3) are consistent with structure **16**: both positive and negative ion spectra show losses of $H_2$ and $CH_2O$. Elimination of $CH_2O$ [eqn. (12)] gives **17** [in this case the



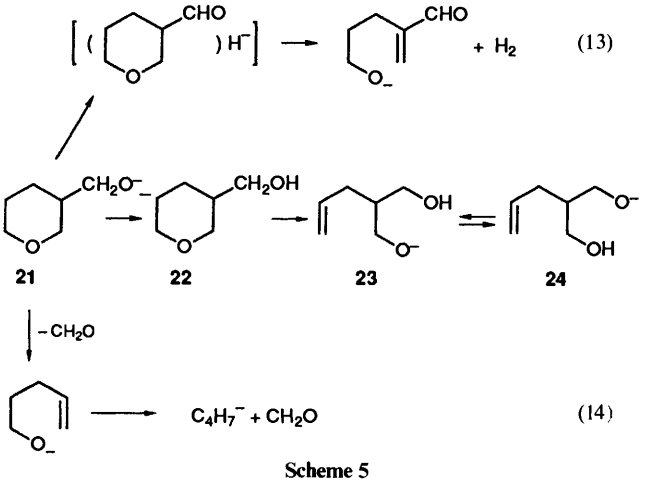

Scheme 3




Scheme 4

negative ion spectrum of this product ion (Table 3) shows losses of $H_2$ and $H_2O$, while the positive ion spectrum gives $C_3H_3{}^+$ as base peak].

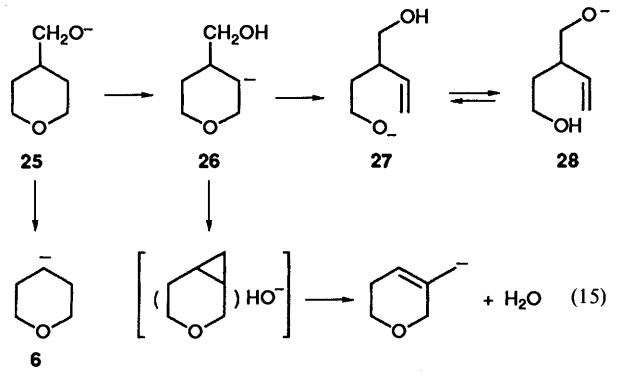
The spectra of the three deprotonated tetrahydropyran methanols are different in a number of major respects (Table 2 and Fig. 2). In the case of the 2-ion **18**, the two oxygen atoms have equilibrated prior to or during decomposition. Initial proton transfer and ring opening followed by subsequent proton transfers would form the equilibrating system **19** ⟹ **20**. Minor, but equal losses of $CH_2O$ (from **19** and **20**) are observed. The major fragmentation is loss of water [*cf.* eqn. (4)] forming an ion which subsequently loses $CH_2O$ (*cf.* Fig. 2 and Table 3).




Scheme 5

The major fragmentations of the 3-isomer **21** are competitive losses of $H_2$ and $CH_2O$. The loss of $H_2$ is not a major feature of either the other isomers or of tetrahydropyran itself. Since (THP-3-$CD_2O^-$) specifically loses HD, **21** must be the decomposing ion as shown in eqn. (13). Ion **21** must also lose $CH_2O$ directly, since (THP-3-$CD_2O^-$) loses $CD_2O$ and $CH_2O$ in the

ratio 10:3. This is shown in eqn. (14): the first formed product ion itself loses $CH_2O$ [Fig. 2, Table 2, *cf.* eqn. (2)]. That these two processes are so pronounced, must be a reflection of their energetics compared with that of the oxygen equilibration process **21** ⟶ **22** ⟶ **23** ⇌ **24** (Scheme 5). Perhaps the energy barrier for the 'cross ring' proton transfer **21** ⟶ **22** is a contributing factor. Even so, the equilibration process still occurs, since there is a minor loss of $H_2O$ which involves both oxygens equally. It is therefore possible that the loss of $CH_2O$ from [THP-3-$CD_2O^-$] may come from ring-opened structure $CH_2$=$CHCH_2CH(CD_2OH)CH_2O^-$ [*cf.* **23** ⇌ **24**]. If this is so, then 40% of the loss of $CH_2O$ from **21** occurs as shown in eqn. (14), with 60% occurring from **23** and **24**.




**Scheme 6**

The 4-isomer **25** mainly loses $H_2O$, but there is minor loss of $CH_2O$. Ion **25**, uniquely in this series, loses both $H_2O$ and $CH_2O$ preferentially from the side chain; only minor loss occurs through ring-opened forms (*e.g.* **27** and **28**) (Table 2, Fig. 2). The direct loss of $CH_2O$ from **25** forms **6** (Scheme 6 and *cf.* Scheme 1). The major loss of $H_2O$ presumably originates from **26** [**25** and **26** show similar fragmentations: compare the spectra of the $(M - D^+)$ and $(M - H^+)$ ions from THP-4-$CD_2OD$ (Table 2)], and we suggest the sequence shown in eqn. (15).

## Conclusions

(i) Tetrahydrofuran and tetrahydropyran deprotonate specifically at the 3-position, and subsequent fragmentation is that of the ring-opened alkoxide. There is no evidence that the 2-anions of the two systems may be formed either directly or indirectly, but it appears that the 4-anion of tetrahydropyran has, at least, transient existence.

(ii) Tetrahydrofuran- and tetrahydropyran-methanols deprotonate preferentially at HO, but minor deprotonation also occurs at the 3-position(s) of the ring. Such systems, at least to some extent, fragment through ring-opened forms. In the particular case of the 'carbohydrate' models, *i.e.* the 2-isomers, ring cleavage of the 3-anion followed by proton transfer gives decomposing ions in which the two oxygens are equivalent.

## Experimental

Collisional activation mass spectra (MS/MS) were recorded using a Vacuum Generators ZAB 2HF mass spectrometer operating in the negative chemical-ionization mode.[20] All slits were fully open to obtain maximum sensitivity and to minimize energy resolution effects.[21] The chemical ionization slit was used in the ion source, ionizing energy 70 eV (tungsten filament); ion source temperature 180 °C, accelerating voltage 7 kV. Deprotonation of all neutrals was effected by $H_2N^-$ (from $NH_3$). The initial measured source pressure of $NH_3$ was $1 \times 10^{-5}$ Torr, 1 Torr = 133.332 Pa. The substrate pressure (liquids introduced through the septum inlet at 150 °C; solids through the direct probe with no heating) was typically measured at $5 \times 10^{-7}$ Torr. The estimated total pressure in the ion source is $10^{-1}$ Torr. The pressure of helium just outside the second collision cell was $2 \times 10^{-7}$ Torr measured by an ion gauge situated between the electric sector and the second collision cell. This produced a decrease in the main beam signal of *ca.* 10%, and corresponds to essentially single collision conditions.

Sequential product ion spectra (MS/MS/MS) and charge reversal[11] MS/MS/MS spectra were measured with a Kratos MS 50 TA instrument previously described.[22] Neutral substrates were deprotonated by $MeO^-$ (from MeONO[23]) in a Kratos Mark IV chemical ionization source ion source temperature 100 °C, electron energy 280 eV, emission current 500 μA and accelerating voltage 8 kV. Samples were introduced through an all glass heated inlet system at 100 °C. The indicated source pressure of substrate was $2 \times 10^{-5}$ and of methyl nitrite $1 \times 10^{-6}$, giving an estimated source pressure of *ca.* $10^{-1}$ Torr. The indicated pressure of helium in the collision cells was $2 \times 10^{-6}$ Torr, giving a decrease in the main beam signal of 30%.

Tetrahydrofuran-2-methanol, tetrahydrofuran-3-methanol and tetrahydropyran-2-methanol were commercial samples. Tetrahydropyran-4-methanol was prepared by reduction of the corresponding carboxylic acid.[24] Tetrahydropyran-3-methanol was prepared from acrolein by a reported method.[25]

*Labelled Compounds.*—All of the $HOCD_2$ derivatives were prepared by reaction of the appropriate carboxylic acid with $LiAlD_4$.[26] Yields 40–70%, $D_2$ = 99%. The corresponding $DOCD_2$ derivatives were formed in the septum inlet system of the mass spectrometer by exchange of the appropriate $HOCD_2$ compound with $D_2O$ ($D_3 \geqslant 90\%$ in all cases).[27]

*Tetrahydrofuran-2-D-methanol.* This was prepared by reduction[26] of methyl 2-D-tetrahydrofuroate[28] with $LiAlH_4$. Yield = 61%; $D_1$ = 99%.

*The $^{18}O$ labelled alcohols.* These were prepared by the following method. A mixture of the appropriate carboxylic acid (2 g) and thionyl chloride (8 $cm^3$) was stirred at 50 °C for 2 h. The thionyl chloride was removed and the acid chloride purified by distillation *in vacuo*. The pure acid chloride (1.0 g) in anhydrous tetrahydrofuran (10 $cm^3$) containing $H_2{}^{18}O$ (300 mg, 24% $^{18}O$) was allowed to stand at room temperature for 4 h, the solvent removed and the residue dried ($CaCl_2$) *in vacuo* (0.02 mmHg) for 2 h. The residue was dissolved in anhydrous tetrahydrofuran (5 $cm^3$), and the mixture was added dropwise over 15 min, under nitrogen, to a stirred suspension of $LiAlH_4$ (500 mg) in tetrahydrofuran (5 $cm^3$). The mixture was heated under reflux for 3 h, cooled to 0 °C, aqueous sodium sulfate (saturated, 5 $cm^3$) was added, and the mixture was extracted with diethyl ether ($3 \times 25$ $cm^3$), dried ($Na_2SO_4$) and distilled *in vacuo* to obtain the labelled alcohol (yield 60–75%, $^{18}O$ = 12%).

## Acknowledgements

J. H. B. and R. N. H., respectively, thank the Australian Research Council and the Midwest Center for Mass spectrometry (an NSF instrumental facility) for financial support. R. A. J. O'H. and S. D. thank the ARC for postdoctoral fellowships.

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*Paper* 2/00808D
*Received* 14*th February* 1992
*Accepted* 13*th April* 1992