$^{13}C,^{13}C$ Spin–Spin Coupling Constants as a Probe for Mesomeric Structures: Vitamin C

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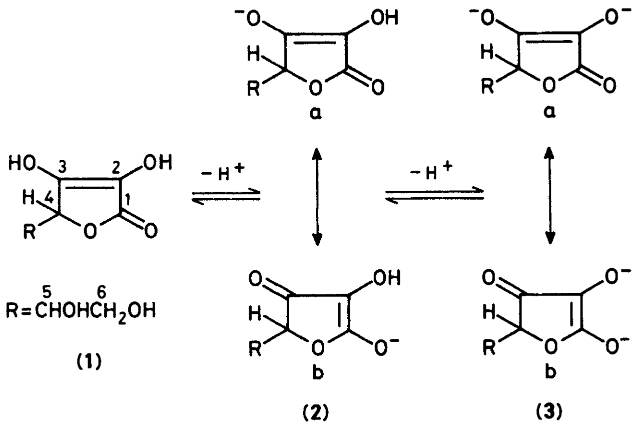
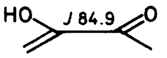
The pH-dependence of the $^{13}C,^{13}C$ spin–spin coupling constants of ascorbic acid indicates which of the mesomeric forms best describes the anion.

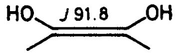
Vitamin C has been shown to exist in solution predominantly as the tautomer (**1**) by ^{13}C chemical shift and $^{13}C,^{1}H$ spin–spin coupling analysis,[1,2] although other forms theoretically are possible.[3] N.m.r. experimental findings have recently been corroborated by MO calculations.[4] On titration of ascorbic acid (**1**) with NaOH first the anion (**2**) is formed and then the dianion (**3**). For (**2**) and (**3**) the mesomeric valence-bond structures (**2a/b**) and (**3a/b**) can be written and their relative contribution to the ground state of the molecules can be discussed. We have addressed this question using $^{13}C,^{13}C$ spin–spin coupling constants.

The $^{13}C,^{13}C$ spin–spin coupling constants of vitamin C have been measured at natural abundance using the INADEQUATE technique[5] in saturated D_2O solution (see Table 1). Since the connectivity of a carbon skeleton is directly seen from the $^{1}J_{CC}$ spin–spin coupling constants the present analysis nicely confirms the chemical shift assignment in the literature.[1,2]





(**4**)



(**5**)

For the α-hydroxy-oxo fragment (**4**) a $^{1}J_{C\text{-}1,C\text{-}2}$ value of 84.9 Hz was found, whereas for the enediol fragment (**5**) the $^{1}J_{C\text{-}2,C\text{-}3}$ value was 91.8 Hz. The large $^{3+2}J_{CC}$ value of 19.5 Hz connecting C-1 with C-3 is remarkable. From our earlier experiments on the behaviour of the ^{13}C chemical shifts upon titration we wondered whether the $^{13}C,^{13}C$ spin–spin coupling values would show a similar pattern. Results of the titration for the spin–spin coupling constants of C-2 with C-1 as well as with C-3 are given in Figure 1; the other $^{1}J_{CC}$ values are not altered significantly upon titration. After addition of NaOH (0.5 equiv.) the two spin–spin coupling constants between C-2 and C-1 or C-3 are identical. Since after addition of 1 equiv. of NaOH they are opposite to the starting values for ascorbic acid, we conclude that the anion is best described by structure (**2b**). The value of 84.5 Hz previously assigned to the α-hydroxy-oxo fragment (**4**) now connects the carbon atoms C-2 and C-3, whereas the spin–spin coupling constant of 91.6 Hz typical for the enediol fragment (**5**) now connects C-1 and C-2. A similar trend can be found in a comparison of the crystal structures of ascorbic acid and of sodium ascorbate[6] where the length of the C-2—C-3 bond increases and the length of the C-1—C-2 bond decreases on formation of the

Table 1. $^{13}C,^{13}C$ Spin–spin coupling constants of ascorbic acid (**1**).[a]

$^{1}J_{C\text{-}1,C\text{-}2}$	84.9	$^{2}J_{C\text{-}1,C\text{-}3}$	19.5
$^{1}J_{C\text{-}2,C\text{-}3}$	91.8		
$^{1}J_{C\text{-}3,C\text{-}4}$	50.8		
$^{1}J_{C\text{-}4,C\text{-}5}$	39.4		
$^{1}J_{C\text{-}5,C\text{-}6}$	42.0		

[a] Values given in Hz, measured for a saturated D_2O solution in D_2O at 305 K. The n.m.r. tubes were purged with nitrogen and sealed with parafilm to exclude oxygen during the typical measurement time of 12 h. The n.m.r. instrument was a Bruker WH-400, equipped with a 80k Aspect 2000 computer and a Diablo series 30 disc drive. The Bruker FTQNMR program version 820601.5 (1983) was used to enable a 32-step phase cycling for the 1-D INADEQUATE measurements. For a more detailed experimental description of similar experiments from this laboratory see ref. 9.

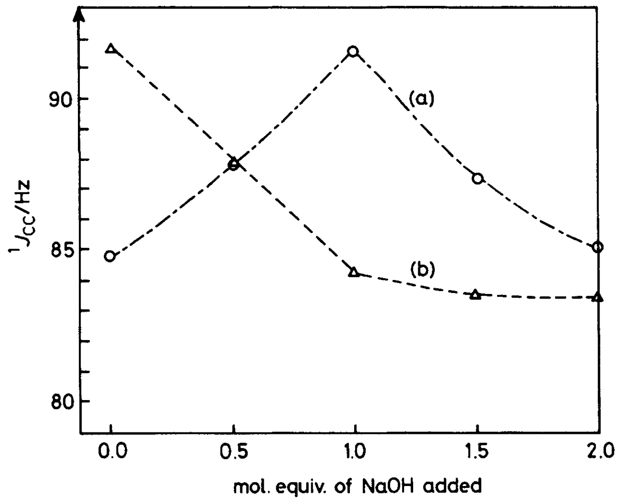


Figure 1. Variation of (a) $^1J_{C\text{-}1,C\text{-}2}$ and (b) $^1J_{C\text{-}2,C\text{-}3}$ on addition of NaOH to ascorbic acid (**1**).

anion. However, in the solid state the C-2—C-3 bond of the anion is still somewhat shorter than the C-1—C-2 bond, contrary to the conclusion deduced from the spin–spin coupling constants. Attempts to explain our findings with INDO calculations of the Fermi contact contribution to the spin–spin coupling constants failed badly.[7] The calculations yield the wrong order for (**1**), and, in addition, the values do not change significantly for the anion, contrary to experiment. Good model compounds for the $^1J_{CC}$ values in the fragments (**4**) and (**5**) are unfortunately not available[8] and the effect of ionisation on $^1J_{CC}$ spin–spin coupling constants has not to our knowledge been investigated.

On further titration the two spin–spin coupling values become similar and show a difference of 2 Hz for the dianion. This could be interpreted to mean that for the dianion (**3**) both structures contribute equally. The lower values compared to (**2**) are probably caused by the second negative charge.

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