

Ring-Chain Tautomerism 'Frozen-out' by Crystal Packing Forces: ^{13}C N.M.R. Spectroscopy and the Remarkable Crystal Structure of the Bromohydrin of 7,7-Dichlorobicyclo[3.2.0]heptan-6-one

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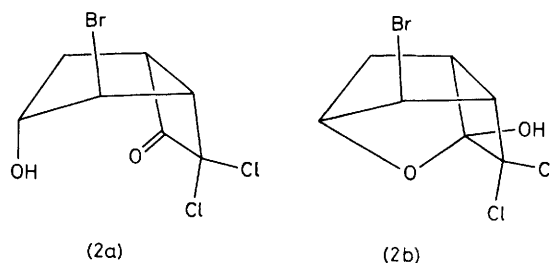
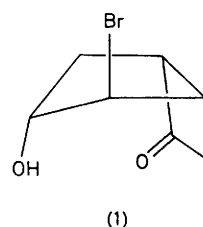
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X-Ray structure analysis of the title compound shows it to exist as a remarkable 1 : 1 mixture (in a single crystal) of ring-chain tautomers and which are detectable by n.m.r. spectroscopy in acidified CHCl_3 as an equilibrium mixture varying between 1 : 1 to 1 : 2.8 over the range 238—304 K.

We have shown that¹ in several bicyclo[3.2.0]heptan-6-one derivatives transannular interactions can occur between a 3-*endo*-nucleophilic substituent and the carbonyl group as in (1). Although all these compounds exist as the ketone there was evidence from the $\text{O} \dots \text{C}=\text{O}$ distance and the related out-of-plane deformation of the carbonyl group that the compounds could all be interpreted as 'frozen-out' intermediates on the reaction pathway described by Bürgi, Dunitz, and Shefter.² Deviations from planarity were, for the most part, small and we wished to study a compound that would show a geometry more distorted from (2a). Activation of a ketone group by electron-withdrawing substituents favours the acetal form and (2) has been reported (on ^1H n.m.r. evidence³) to exist as a *ca.* equimolar mixture of (2a) and (2b).

The X-ray crystal structure of the solid which crystallises from CCl_4 solution of (2) at room temperature is reported here.

Crystal data: $\text{C}_7\text{H}_7\text{BrCl}_2\text{O}_2$, $M = 273.95$, monoclinic, space group $\text{C}2/c$, $Z = 16$, $a = 22.98(5)$, $b = 12.05(3)$, $c = 14.41(3)$ Å, $\beta = 107.78(2)^\circ$, $F(000) = 2144$, $\mu(\text{Mo-K}\alpha) = 47.06 \text{ cm}^{-1}$. 1596 reflections with $I > 3\sigma(I)$ were collected on a Stoe 2-circle diffractometer. The structure was solved by direct



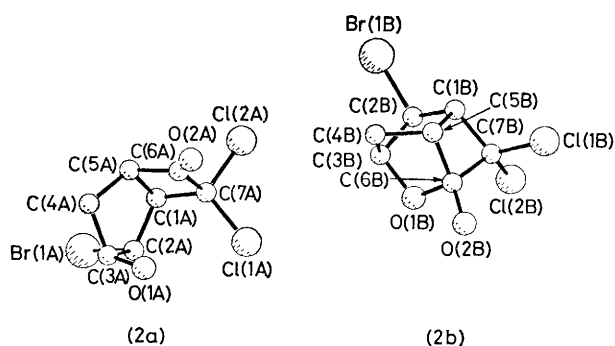


Figure 1

methods and Fourier methods. The structure was refined to $R = 0.053$ by full-matrix least-squares with anisotropic thermal parameters. Isotropic hydrogen atoms were included in the refinement.† The structure is hydrogen bonded [O(1A) . . . O(2B) = 2.979 Å ($x, -y, z-0.5$); O(2B) . . . O(2A) = 2.836 Å ($0.5-x, 0.5-y, -z$)] and contains two molecules in the asymmetric unit (Figure 1). There is no evidence for disorder. Remarkably, the two independent molecules correspond to (2a) and (2b). Their molecular geometries show little distortion along the reaction pathway (2a) . . . (2b); the O . . . C=O length is 2.83(2) Å in (2a) and 1.43(1) Å in (2b). The expected out-of-plane displacement of the carbonyl group in (2a) is masked by experimental error.

It appears, therefore, that crystal packing forces, whilst not strong enough to trap an intermediate, have isolated both partners in a chemical equilibrium. Though frequently seen in conformational processes, this is unusual for chemical reactions involving bond formation and is normally limited to proton exchange (*e.g.* in anthranilic acid where both the neutral molecule and zwitterion coexist in the crystal⁴).

To our knowledge, this is the first example of ring-chain tautomers being isolated as partners in a crystal lattice. For (2), it seems that a crystal structure of (2a) + (2b) is more stable than either (2a) or (2b) provided that we can be sure that (2a) and (2b) are equilibrating in solution and that crystallisation gives the thermodynamically controlled product. Although the last point can never be formally verified, differential scanning calorimetry of the crystals showed no phase transitions in the range 173 to 352 K (m.p.). The ¹³C n.m.r. spectrum of crystals of (2) in CHCl₃ solution shows 14 resonances consistent with an equimolar mixture of (2a) and (2b). The spectrum appears independent of temperature sug-

† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

Table 1. Chemical shift data (p.p.m. to high frequency of Me₄Si) at ambient temperature in absence of acid in CDCl₃.

Ketone		Hemiacetal	
Position	Assignment	Position	Assignment
196.62 s	C(6)	103.90 s	C(6)
87.38 s	C(7)	89.13 s	C(7)
80.56 d	C(3)	85.52 d	C(3)
60.42 d	C(1), C(2), C(5)	54.52 d	C(1), C(2), C(5)
59.49 d		47.16 d	
52.45 d		46.99 d	
36.18 t	C(4)	32.97 t	C(4)

gesting that the interconversion of (2a) and (2b) is very slow and that the 1:1 composition is determined by the stoichiometry of the crystal. Addition of a trace of acid catalyst (*p*-MeC₆H₄SO₃H) markedly altered the spectrum giving a non-integral ratio which was temperature dependent. From the integrated intensities of the pairs of resonances (*e.g.* 195.5 (C=O) and 104.1 p.p.m. [C(OR)(OH)] or 33.0 [C(4B)] and 36.2 p.p.m. [C(4A)]); in inverse gated decoupling experiments, an estimate of the acetal/ketone ratio at different temperatures was made (300 K, 1.0:1.0; 273 K, 1.0:1.7; 253 K, 1.0:2.0; 238 K, 1.0:2.8). Increasing the concentration of the acid or raising the temperatures led, as expected, to coalescence of peaks with (2a) ⇌ (2b) becoming rapid on the n.m.r. time scale.

Recrystallisation of (2) from a number of solvents (MeOH, MeCN, MeNO₂, CHCl₃, CCl₄, with and without acid catalysts) always led to the same solid. This was verified by i.r. spectroscopy since the spectrum of (2a) + (2b) in a KBr disc is very characteristic with a double peak on the OH region (3380 and 3480 cm⁻¹). The crystal morphology and melting points were also used as checks.

This is evidence that despite the composition of the solution, packing forces control the crystal structure and stoichiometry of the solid. There are no unusual features in the intermolecular contacts and there is no reason why similar frozen-out chemical equilibria should not be observed in other crystals.

One of us (R. G.) thanks the S.R.C. and Glaxo Group Research (Ware) Ltd. for a CASE studentship.

Received, 18th August 1981; Com. 1009

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