

## Kinetics of Hydrogen Isotope Exchange Reactions. Part XXX.<sup>1</sup> Steric Course of $\gamma$ -Radiation-induced Exchange between Water and Tartaric Acids

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$\gamma$ -Irradiation of solutions of (+)-tartaric acid and of *meso*-tartaric acid in tritiated water at pH 7 leads to an exchange of carbon-bonded hydrogen with the solvent. For each substrate the exchange proceeds to an approximately equal extent with inversion and with retention of configuration. The results support the conclusions of a similar stereochemical study on *cis*- and *trans*-cyclohexane-1,2-diols.

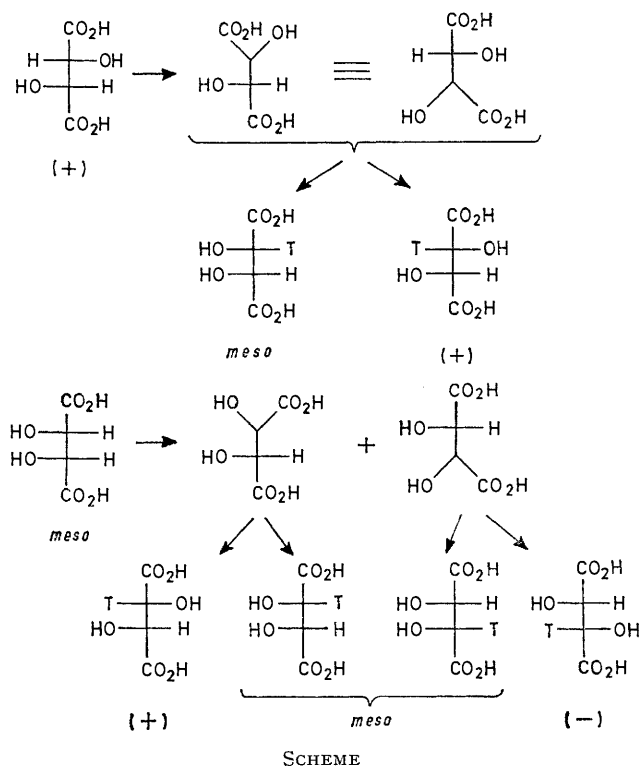
In parallel with experiments on the steric course of radiation-induced exchange of C-H bonds in cyclohexane-1,2-diols,<sup>2</sup> a corresponding study was carried out with tartaric acids. Because tartaric acid contains carbon-bonded hydrogen atoms only at the two chiral centres, it was hoped that its study would provide more accurate information on the stereochemical outcome of radiation-induced hydrogen exchange. In practice the system proved to be much less convenient and the results were mechanistically less informative than those obtained with cyclohexanediols. In general terms, they are consistent with the conclusions drawn from that study and, to that extent, offer support for the mechanism proposed.

We find that  $\gamma$ -radiolysis of (+)-tartaric acid in presence of tritiated water leads to formation of labelled (+)- and *meso*-tartaric acid in the approximate ratio 1:1. Correspondingly, radiolysis of *meso*-tartaric acid leads to a similar ratio (53:47) of labelled racemic to *meso*-tartaric acid. These figures suggest no discrimination in favour of or against the formation of the labelled *meso*-acid from either substrate. In each case, the formation of unchanged substrate corresponds to retention of configuration accompanying exchange and the formation of the other product corresponds to inversion at one of its two chiral centres. Because only a small fraction of the substrate undergoes reaction (even after allowing for the fact that exchange without incorporation of tracer is several powers of ten faster than the observable tritium exchange), it is considered permissible to ignore the occurrence of two successive exchange reactions which could lead to inversion at both chiral centres.

In the light of previous findings, these results again point to a common intermediate in the formation of both products from either precursor, and suggest that this intermediate is formed by hydrogen abstraction. On this view the two reactions can be written (in terms of Fischer projections) as shown in the Scheme.

On the basis of evidence obtained with other substrates we assume that conversion of the radical formed with one of the isomeric tartaric acids proceeds in the

spur region *via* electron capture by the radical and subsequent neutralisation of the carbanion by proton (triton) transfer from the solvent. There is little direct evidence for these aspects of the mechanism with tartaric acid, and the presence of anionic carboxylate



groups in the substrate opens the possibility that the steps subsequent to the formation of the radical may differ in detail from the route proposed for dioxan<sup>1</sup> and cyclohexanediols.<sup>2</sup>

The observation that the products with inversion and with retention of configuration are formed in almost equal amount implies that there is little or no steric preference in the reactions which lead from the radical back to acid. This result stands in contrast to the finding with cyclohexanediols where there is a distinct preference for formation of the *trans*-isomer. The

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<sup>1</sup> Part XXIX, V. Gold and M. E. McAdam, *Proc. Roy. Soc. (A)*, in the press.

<sup>2</sup> J. P. Garvey, V. Gold, M. E. McAdam, and A. Cooper, *Proc. Roy. Soc. (A)*, in the press.

difference can be rationalised as follows. The radical or carbanion from tartaric acid is less constrained than the cyclic radical or anion from cyclohexanediols. In the latter case neutralisation of the anion to give cyclohexanediol is somewhat selective<sup>2</sup> because there may be both a pronounced conformational preference in the anion as well as a marked difference in the ease of approach of solvent to the carbanion centre and, hence, of its ease of neutralisation by proton (triton) transfer from solvent.

Two similar pairs of experiments were carried out with addition of sodium nitrate (an electron scavenger,  $k_{\text{NO}_3^-} = 1.1 \times 10^{10} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ )<sup>3</sup> and sodium thiocyanate (a hydroxyl radical scavenger,  $k_{\text{SCN}^-}^{\text{OH}} = 1.1 \times 10^{10} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ )<sup>4</sup>. In each experiment it was found that the extent of labelling of starting material

contributions are altered by slight pH changes, and whether they are significantly different for the isomers because of the  $pK$  differences between them.

Of course, this particular difficulty could be avoided by working with the dimethyl esters of the tartaric acids, but experiments with esters were found to suffer from other disadvantages, especially the occurrence of radiation-induced exchange in the ester group.

#### EXPERIMENTAL

Stock solutions of (+)-tartaric acid (B.D.H. AnalaR, >99.5%) and of *meso*-tartaric acid (B.D.H., >99%) were prepared by weight and the pH values were adjusted to 7.0 by addition of sodium hydroxide solution; any additional solutes and tritiated water (3 ml; diluted tritiated

#### Summary of experiments

[HTO] = 33.4 Ci dm<sup>-3</sup>; irradiation dose = 1.45 Mrad; sample volume = 13 cm<sup>3</sup> (For each experiment the upperline relates to the tritium assay of the dimethyl ester of the substrate and the bottom line to the dimethyl ester of the carrier)

Expt. no.	Substrate (carrier)	Weight g	Added substance	Conc. M	Wt. counted		Efficiency	C.p.m.	$G_{\text{ex}}$
					mg				
1	+	1.003			48.3	0.560	46 540	0.157	
	( <i>meso</i> )	1.123			12.5	0.545	10 680	0.160	
2	+	1.003	KNO <sub>3</sub>	0.042	8.5	0.592	2 950	0.053	
	( <i>meso</i> )	1.130			11.4	0.583	4 580	0.071	
3	+	1.003	NaSCN	0.084	3.0	0.592	877	0.045	
	( <i>meso</i> )	1.226			4.0	0.583	717	0.034	
4	<i>meso</i>	0.997			10.8	0.566	7 505	0.111	
	(±)	1.015			5.3	0.595	4 260	0.125	
5	<i>meso</i>	0.997	KNO <sub>3</sub>	0.053	5.8	0.579	833	0.022	
	(±)	1.001			9.3	0.594	1 025	0.017	
6	<i>meso</i>	0.997	NaSCN	0.077	10.9	0.584	8 485	0.121	
	(±)	1.002			19.0	0.595	12 965	0.104	

was approximately equal to that of the inversion product. It was also found in almost every case that there was less incorporation of tritium under these conditions, but the extent to which the exchange reaction was depressed by addition of scavengers was not regular and would require further study. As was stated at the outset, the tartaric acid system is not a convenient one. It is therefore possible that the irregular results obtained with scavengers arise from a low reproducibility of conditions between different samples, although pairs of results obtained on the *same* sample were mutually consistent. It is possible that one of our difficulties was inadequate buffering of the solutions, since pH was adjusted to 7 by addition of sodium hydroxide to tartaric acid (an only moderately 'weak' acid). In this connection it may also be relevant that at 25° the *meso*-form is a slightly weaker acid ( $pK_1$  3.22;  $pK_2$  4.82)<sup>5</sup> than the optically active isomers ( $pK_1$  3.04;  $pK_2$  4.36).<sup>6</sup> At pH 7 the predominant species is in both cases the dianion, but it is impossible to say how much each form (acid, monoanion, dianion) of a substrate contributes to the total reaction, whether these

water obtained from Radiochemical Centre, Amersham) were added to an aliquot portion (10 ml) of this stock. After being de-gassed, the solutions were irradiated by the cobalt-60 source at Imperial College, at a stated dose rate of 156 rad s<sup>-1</sup>. For sample isolation and analysis the content of the reaction vessel was transferred to a flask containing *ca.* 1 g of the appropriate carrier [*meso*-acid in the case of (+)-acid as reactant; (±)-acid when *meso*-acid was the reactant], and water was removed under reduced pressure. The residue was dissolved in methanol (30–40 cm<sup>3</sup>) and the methanol was then taken off in a rotary evaporator; this operation was repeated a large number of times at different stages of the subsequent treatment, in order to remove all traces of hydroxy-bound tritium or residual water, as indicated by constant activity of the residue. The residue was dissolved in water and the solution was adjusted to pH 7 with sodium hydroxide. An equivalent amount of silver nitrate was added and the precipitated silver salts were filtered off and dried under reduced pressure. To prepare the methyl tartrates, the silver salts were refluxed (6 h) in methanol solution containing a five-fold excess of methyl iodide. Iodine was removed from the separated solid residue by sublimation. The isomeric esters in each specimen were then separated by g.l.c. (F and M model 770/775; SE-30 column) and their activities subsequently assayed.

<sup>3</sup> M. Anbar, M. Bambenek, and A. B. Ross, Nat. Stand. Ref. Data Ser., Nat. Bur. Stand. U.S.A., 1973, vol. 43.

<sup>4</sup> L. M. Dorfman and G. E. Adams, Nat. Stand. Ref. Data Ser., Nat. Bur. Stand. U.S.A., 1973, vol. 46; D. H. Ellison, G. A. Salmon, and F. Wilkinson, Proc. Roy. Soc. (A), 1972, **328**, 23.

<sup>5</sup> G. H. Jeffery and A. I. Vogel, J. Chem. Soc., 1934, 1101.

<sup>6</sup> R. G. Bates and R. G. Canham, J. Res. Nat. Bur. Stand., 1951, **47**, 343.

The procedures for de-gassing, irradiation, and counting, and the method of calculating  $G_{\text{ex}}$  have been described in earlier parts.<sup>3,7</sup>

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<sup>7</sup> C. L. Brett and V. Gold, *J.C.S. Perkin II*, 1973, 1437.

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