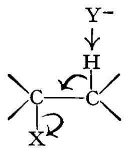
464. cis-*Elimination in Thermal Decompositions.*

By D. H. R. Barton.

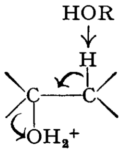
It is emphasised that thermal elimination reactions of the unimolecular type must involve a four-centre planar transition state and that, as a consequence, such reactions must be stereochemically specific in requiring a *cis*-configuration of the eliminated groups. This generalisation is illustrated by reference to the thermal decompositions of methyl xanthates and of benzoates in the terpenoid and the steroid field respectively. It is suggested that the concept of *cis*-elimination in this type of reaction provides a useful method for the elucidation of stereochemical relationships. In particular, it confirms the assignment of configuration at the 7-position in steroids recently made by Fieser, Fieser, and Chakravarti (*J. Amer. Chem. Soc.*, 1949, **71**, 2226). Configurations are assigned to *iso*thujyl alcohol and to *neoiso*thujyl alcohol.

It has long been recognised that addition to olefinic linkages by ionic mechanisms, in the absence of complicating factors, proceeds in the *trans*-sense. More recently the corresponding requirement of *trans*-elimination through heterolytic E_2 reaction mechanisms has become generally accepted (see Hughes, Ingold, *et al.*, *J.*, 1948, 2093). The transition state in reactions of this type is pictured as in (A), where X indicates the eliminated negative ion and Y the attacking nucleophilic reagent. From the stereochemical point of view this *trans*-type of ionic elimination has been very well illustrated by the acid-catalysed dehydrations of cyclic alcohols (see *inter al.*, Zeitschel and Schmidt, *Ber.*, 1926, **59**, 2298; Hückel *et al.*, *Annalen*, 1930, **477**, 99; Vavon and Barbier, *Bull. Soc. chim.*, 1931, **49**, 567; Price and Karabinos, *J. Amer. Chem. Soc.*, 1940, **62**, 1159). Presumably the transition state in reactions of this type is as illustrated in (B) where R is H or the alicyclic radical of the alcohol being dehydrated.

There is, however, another important type of elimination mechanism which is stereochemically specific in the *cis*-sense, and which has not yet received adequate recognition. This mechanism is illustrated by those olefin-forming thermal decomposition reactions which occur homogeneously and are unimolecular.* Thus the pyrolyses of ethyl chloride, 1 : 1-dichloroethane, *iso*propyl chloride, and *tert.*-butyl chloride all proceed by the unimolecular mechanism giving hydrogen chloride and the corresponding olefin (Barton and Howlett, this vol., p. 165; Barton and Onyon, *Trans. Faraday Soc.*, 1949, **45**, 725; Barton and Head, forthcoming publication). The transition state in these reactions, shown in (C), is a specific example of the four-centre type of problem (compare Sherman, Quimby, and Sutherland, *J. Chem. Physics*, 1936, **4**, 732). It is a characteristic of the latter that the four centres must lie, suitably disposed with respect to each other, in one plane to ensure the minimisation of the activation energy (Glasstone, Laidler, and Eyring, " The Theory of Rate Processes," McGraw-Hill, 1941, p. 90) and, therefore, *cis*-stereochemistry *must* be demanded in the reactant. This deduction applies quite generally to unimolecular thermal decomposition reactions.



(A.)



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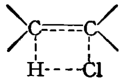
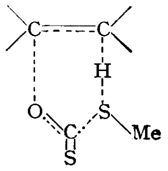


(C.)



(D.)

The most extensive evidence in this connection is provided by the experiments of Hückel, Tappe, and Legutke (*Annalen*, 1940, **543**, 191) on the stereochemical specificity of Tschugaeff's xanthate reaction. The latter is a process involving the thermal decomposition of the methyl xanthates of alcohols, suitably alicyclic alcohols, to give carbon oxysulphide, methanethiol and the corresponding olefin (Tschugaeff, *Ber.*, 1899, **32**, 3332; compare McAlpine, *J.*, 1932, 912); the transition state may be represented as in (D). The results are summarised in the table. Also included in this table are data for a number of other methyl xanthates, the decompositions of which have been described in the literature. Thus (—)-pinocampheol (VI) (Schmidt, *Ber.*, 1944, **77**, 544) methyl xanthate decomposes to give mainly δ-pinene (IX) (Gildemeister and Köhler, *Wallach Festschrift*, 1909, 414; compare Tschugaeff, *J. Russ. Phys. Chem. Soc.*, 1907, **39**, 1330) instead of the alternative α-pinene (X). Also (—)-*neo*thujyl alcohol (VII) (Short and Read, *J.*, 1938, 2016; 1939, 1040) furnishes, as the methyl xanthate, β-thujene (XI) (Tschugaeff and Fomin, *Ber.*, 1912, **45**, 1293) and not α-thujene (XII). Since, however, the latter hydrocarbon is obtained by the pyrolysis of the methyl xanthate of (+)-*iso*thujyl alcohol (*idem, J. Russ. Phys. Chem. Soc.*, 1910, **42**, 497), this alcohol must now be assigned the configuration shown in (VIII) (compare Short and Read, *loc. cit.*), whilst *neoiso*thujyl alcohol must be its hydroxylic epimer.

Methyl xanthate from :	Formula. *	Relation of OH to bridgehead H.	Elimination, %. Towards bridgehead.	Elimination, %. Away from bridgehead.
(—)-Menthol	(I)	*cis*	~70	~30
(+)-*neo*Menthol	(II)	*trans*	~20	~80
trans-α-Decalol (m. p. 49°)	(III)	*trans*	~20	~80
trans-α-Decalol (m. p. 63°)	(IV)	*cis*	~80	~20
cis-α-Decalol (m. p. 93°)	(V)	*trans*	~10	~90
(—)-Pinocampheol	(VI)	*trans*	—	Main product
(—)-*neo*Thujyl alcohol	(VII)	*trans*	—	Main product
(+)-*iso*Thujyl alcohol	(VIII)	*cis*	Main product	—

* Formulæ (I), (II), and (VI) are represented in the correct *absolute* stereochemical arrangements (see Fredga and Miettinen, *Acta Chem. Scand.*, 1947, **1**, 371). Dotted bonds project *below* the plane of the paper.

In all the cases so far considered *cis*-elimination has been feasible, in principle, in a direction away from the bridgehead. It is of interest, therefore, to establish the reason for preferential *cis*-elimination towards the bridgehead when this is stereochemically possible. It is now

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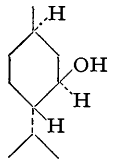
* It is important to distinguish between the use of the word unimolecular as employed by Hughes, Ingold, and their collaborators for certain heterolytic reactions, occurring in solution, and unimolecular as generally employed in speaking of certain gas reactions. In this paper the word is used exclusively in the latter sense.

universally recognised that the homolytic bond dissociation energies of C–X bonds, where X = H, OH, Cl, Br, I, etc., diminish markedly in the series primary, secondary, tertiary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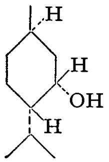
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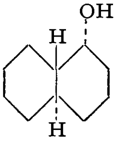
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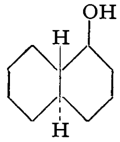
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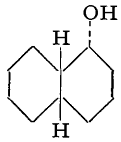
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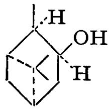
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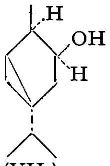
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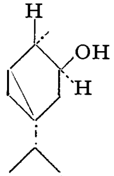
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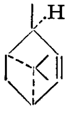
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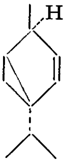
(X.)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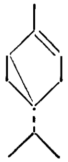
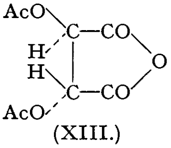

(XII.)

(compare Steacie, " Atomic and Free Radical Reactions," pp. 77 *et seq.*, A.C.S. Monograph No. 102, 1946). It would be expected, therefore, that unimolecular elimination of H–X should also proceed with decreasing activation energy in the series $-\mathrm{C}{-}\mathrm{X} > \rangle\mathrm{C}{-}\mathrm{X} > \rangle\!\!\!-\mathrm{C}{-}\mathrm{X}$. It is well illustrated by the series $CH_3{\cdot}CH_2Cl$ (E_A, 60·8 kcals.) > $(CH_3)_2CHCl$ (E_A, 50·5 kcals.) > $(CH_3)_3{\cdot}CCl$ (E_A, 41·4 kcals.), which we have already established (Barton *et al.*, *loc. cit.*). The same conclusion, of course, applies for the elimination of H–X in the series $-\mathrm{C}{-}\mathrm{H} > \rangle\mathrm{C}{-}\mathrm{H} > \rangle\!\!\!-\mathrm{C}{-}\mathrm{H}$. Here the X grouping is the same throughout and is attached to the neighbouring carbon atom. The latter is secondary in the alicyclic compounds considered in this paper. Amongst compounds listed in the table it is significant that the methyl xanthate of (+)-*iso*thujyl alcohol decomposes at a much lower temperature (130°) than that of (–)-*neo*-thujyl alcohol (183°). Since the non-exponential terms of unimolecular thermal decompositions of the type under consideration here are normally within a power of 10 of 10^{13} (see Barton and Head, forthcoming paper), these decreases in activation energy are the main factor influencing the reaction velocity and thus explain the preferential elimination towards the bridgehead.

Although the deacylation and dehydration reactions which are discussed below have not been proved, except by the stereochemical requirements of *cis*-elimination, to be unimolecular, it is very probable by analogy that they do have this characteristic. Thus the thermal decompositions of *tert.*-butyl acetate and *tert.*-butyl propionate (Rudy and Fugassi, *J. Phys. Colloid Chem.*, 1948, **52**, 357; Warrick and Fugassi, *ibid.*, p. 1314) are of this type, as are the thermal dehydrations of *tert.*-butyl and *tert.*-amyl alcohols (Schultz and Kistiakowsky, *J. Amer. Chem. Soc.*, 1934, **56**, 395).

Amongst the thermal decomposition reactions of acylates to give olefin and carboxylic acid, the pyrolysis of the diacetate of tartaric anhydride (XIII) should be mentioned. This reaction gives, as final product, C_3O_2 (Ott, *Ber.*, 1914, **47**, 2391; Ott and Schmidt, *ibid.*, 1922, **55**, 2126), but it undoubtedly proceeds *via* acetoxymaleic anhydride (XIV) (Hurd, " The Pyrolysis of Carbon Compounds," 1929, p. 536) and therefore must involve *cis*-elimination.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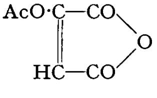
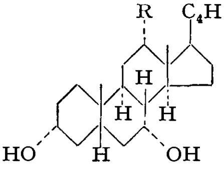
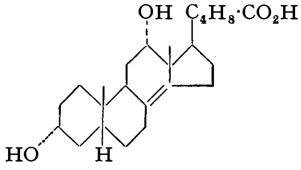

(XIV.)

Some important examples of *cis*-elimination have been discovered in the steroid field. In cholic acid (XV; R = OH) the 7-hydroxyl has been proved, from degradational experiments by Windaus and von Schoor (*Z. physiol. Chem.*, 1925, **148**, 225; compare Iwasaki, *ibid.*, 1936, **244**, 181) on the related chenodeoxycholic acid (XV; R = H), to possess the (α)-orientation, *i.e.*, to lie in the *trans*-relationship to the $C_{(8)}$-hydrogen atom. As is well known, cholic acid is very sensitive to acid dehydrating agents (compare Grand and Reichstein, *Helv. Chim. Acta*, 1945, **28**, 344), *trans*-elimination occurring with initial formation of the corresponding Δ^7-acid.

Depending on the conditions, the latter may be isomerised to the corresponding $\Delta^{8(14)}$-acid, apocholic acid (XVI). As we have pointed out previously (Barton, *J.*, 1946, 1116), unsaturated bile acids with the ethylenic linkage in the 7(8), 8(9), or 8(14) positions cannot be hydrogenated except under drastic conditions. Now, when cholic acid is pyrolysed it affords, as main product, " α "-cholatrienic acid which must be formulated as (XVII), since it is easily hydrogenated (compare below) to the saturated cholanic acid (XVIII) (Wieland and Weil, *Z. physiol. Chem.*, 1912, **80**, 287). The formation of the Δ^6-ethylenic linkage is a demonstration of *cis*-elimination The pyrolysis of apocholic acid affords " β "-cholatrienic acid (XIX), which in contrast is hydrogenated to " β "-cholenic acid (XX) (Borsche and Todd, *Z. physiol. Chem.*, 1931, **197**, 173; Wieland and Deulofeu, *ibid.*, 1931, **198**, 127). Similarly, chenodeoxycholic acid (XV; R = H) readily loses water by ionic *trans*-elimination to give olefinic acids which cannot be hydrogenated (Takahashi, *ibid.*, 1938, **255**, 277; Yamasaki and Takahashi, *ibid.*, 1938, **256**, 21) but on pyrolysis it affords by *cis*-elimination chenocholadienic acid (XXI), which is readily hydrogenated to (XVIII) (Wieland and Reverey, *ibid.*, 1924, **140**, 186).



(XV.)



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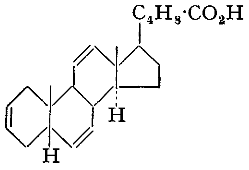
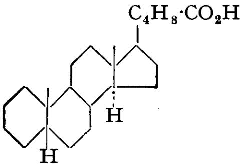


(XVII.)



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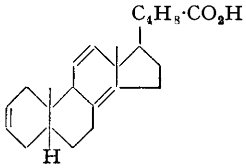

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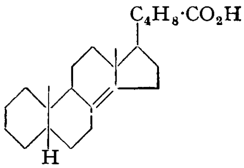

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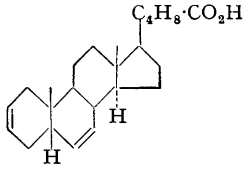
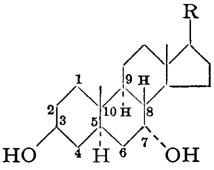


(XXI.)



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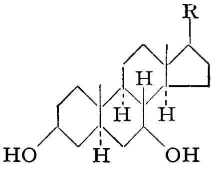

(XXIII.)

The question of the configuration at the 7-position in steroids of the *allo*cholane series has long been a subject for discussion. Wintersteiner and Moore (*J. Amer. Chem. Soc.*, 1943, **65**, 1507) recognised that 7" α "-hydroxycholestanyl acetate was much more resistant to ionic dehydration than the 7" β "-epimer. Recently Fieser, Fieser, and Chakravarti * (*ibid., loc. cit.*) have compared the reactivity of these epimers towards phosphorus oxychloride in pyridine solution. Whereas, the 7" β "-isomer was smoothly dehydrated to cholest-7-en-3(β)-yl acetate (compare Buser, *Helv. Chim. Acta*, 1947, **30**, 1385) the 7" α "-isomer gave the corresponding 7-chloro-compound. This is exactly comparable to the behaviour of (—)-menthol and (+)-*neo*-menthol with phosphorus pentachloride (Zeitschel and Schmidt, *loc. cit.*). The former gives the corresponding chloride but the latter (*trans*-elimination) affords *p*-menth-3-ene. Fieser, Fieser, and Chakravarti concluded, therefore, that the trivial indices at the 7 position should be inverted. This is also in agreement with the (possibly ambiguous) optical rotation evidence discussed by Plattner and Heusser (*Helv. Chim. Acta*, 1944, **27**, 748). Finally, this assignment of configuration is confirmed by pyrolysis evidence. Whereas the 7-benzoate 3-acetate of the 7" β "-epimer (XXII; R = C_8H_{17}) furnished cholest-6-en-3(β)-yl acetate by *cis*-elimination of benzoic acid, the corresponding derivative of the 7" α "-epimer (XXIII) gave cholest-7-en-3(β)-yl acetate (Barton and Rosenfelder, *J.*, in the press).

A similar inversion of trivial indices is required for the 7-position in 7-hydroxycholesterol and analogous compounds. Thus the 7" α "-benzoyloxy-derivative of cholesteryl acetate

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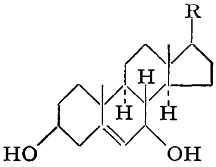
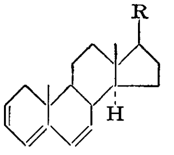
* We are very much indebted to Professor L. F. Fieser for a copy of this paper before publication.

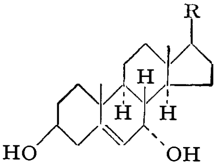
readily gives 7-dehydrocholesteryl acetate on pyrolysis. The parent diol must therefore be 3(β) : 7(β) as in (XXIV; R = C_8H_{17}). On the other hand, the pyrolysis of the epimeric 7" β "-benzoyloxy-compound (Wintersteiner and Ruigh, *J. Amer. Chem. Soc.*, 1942, **64**, 2453) gives what must now be formulated as cholesta-2 : 4 : 6-triene (XXV; R = C_8H_{17}), and therefore the parent diol must be 3(β) : 7(α) as in (XXVI; R = C_8H_{17}).* This is in agreement with the optical rotation evidence (Bide, Henbest, Jones, and Wilkinson, *J.*, 1948, 1788). A similar situation obtains in the derivatives of 3(α) : 7-dihydroxycholest-5-ene which have been studied by Windaus and Naggatz (*Annalen*, 1939, **542**, 204), although here configurations cannot be assigned on the basis of the optical-rotation evidence. The 3(α) : 7" α "-dibenzoate furnished (XXV; R = C_8H_{17}) on pyrolysis, whereas the 3(α) : 7" β "-dibenzoate split out benzoic acid to give 7-dehydro*epi*cholesteryl benzoate. The trivial indices are, therefore, correctly assigned, and the dibenzoates are 7(α) and 7(β) respectively.



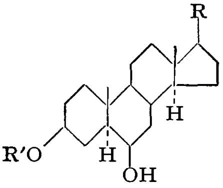
(XXIV.)



(XXV.)



(XXVI.)



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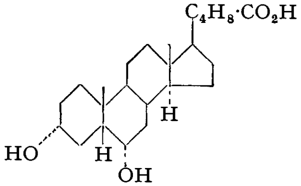

(XXVIII.)

The pyrolysis of the 6-benzoate of 3(β)-acetoxycholestan-6(β)-ol (XXVII; R = C_8H_{17}, R' = Ac) also proceeds, as expected, by *cis*-elimination to give cholest-6-en-3(β)-yl acetate. Another example involving the 6-position is the pyrolysis of hyodeoxycholic acid (XXVIII) which affords what must now be regarded as chola-2 : 6-dienic acid, because it is hydrogenated to give cholanic acid (XVIII) in about 90% yield (Windaus and Bohne, *Annalen*, 1923, **433**, 278). Had the pyrolysis product been chola-4 : 6-dienic acid (Wieland *et al.*, *Z. physiol. Chem.*, 1936, **241**, 47) or an acid with a Δ^5-ethylenic linkage then a major proportion of *allo*cholanic acid would have been expected on hydrogenation.

It will be clear from the examples discussed above that the concept of *cis*-elimination in unimolecular pyrolyses can play as useful a role in elucidating stereochemical relationships as has been played in the past by the idea of *trans*-elimination in many ionic reactions.

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* The alternative formulation for the cholestatriene with the ethylenic linkages at the 3 : 5 : 7-positions (compare Windaus and Naggatz, *Annalen*, 1939, **542**, 204) is actually excluded by the absorption-spectrum evidence. The 2 : 4 : 6-triene should absorb at 310 mμ. in ether, the 3 : 5 : 7-triene at 320 mμ. (Fieser, Fieser, and Rajagopalan, *J. Org. Chem.*, 1948, **13**, 800). The triene obtained by pyrolysis had λ max. at 302 mμ. in ether (Eckhardt, *Ber.*, 1938, **71**, 461).