The Vapour Pressure of Enantiomers and of their Mixtures

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The vapour pressure of a racemic mixture forming a conglomerate is exactly twice that of the pure enantiomers; that of a crystalline racemic compound may be higher or lower than that of the enantiomers, and depends chiefly on the enthalpy and temperature of decomposition of the 1 : 1 adduct.

Since the time of Schroeder and Roozeboom, condensed phase diagrams of chiral compounds have been thoroughly investigated in connection with the study of resolution processes.[1] This is not true for equilibria involving the vapour phase, in spite of the potential interest of sublimation as a method to enhance the optical purity of partially resolved compounds: very few examples are known[1b—3] and a comprehensive and quantitative approach to this subject is still lacking.

This paper discusses the pressure–temperature (p–T) projection diagrams of pure enantiomers, enantiomer mixtures forming a conglomerate, and mixtures forming a crystalline racemic compound. The T–x and p–x diagrams and the related equations will be published in detail elsewhere.[4]

The theoretical p–T diagram of pure enantiomers is shown in Figure 1 (curve A′–A–L), where the A′–A branch corresponds to the solid–vapour equilibrium, point A to the melting point, and curve A–L to the liquid–vapour equilibrium. The slopes of curves A′–A and A–L are related to the enthalpies of sublimation and vaporization, in accordance with the Clausius–Clapeyron equation. The almost vertical line starting from A corresponds to the solid–liquid equilibrium in the absence of the gas phase. In this respect, enantiomers do not differ from other pure chemical substances.

In the liquid phase and under ideal conditions both the pure enantiomers and their mixtures of any composition possess, at a given temperature, the same vapour pressure. As a consequence, the vaporization of such mixtures is a congruent transition (no variation in enantiomeric purity occurs during distillation[1b]); the system is univariant and is always represented in the p–T diagram by the A–L line. This line proceeds with a continuous slope below A until reaching the quadruple point Q [Figure 1(a)], the melting point of the conglomerate, *i.e.* the lowest temperature at which the liquid phase can exist. The vapour pressure of the liquid phase at Q equals that of the solid conglomerate and is exactly *twice* that of the pure crystalline enantiomers at the same temperature. The E–Q curve, which represents the vapour pressure of the conglomerate below T_Q, has the same temperature coefficient as the vapour pressure of the single enantiomers (curve A–A′), but *is shifted above by a factor of two.* This was first pointed out by Meyerhoffer 80 years ago,[5] but his observation remained almost completely ignored.

The vapour pressure of partially resolved samples follows the curves E–Q–A–L: at temperatures lower than T_Q the composition of the vapour phase is racemic and an increase of enantiomeric purity in the residue after partial sublimation can be observed.

The vapour pressure of systems forming crystalline racemic compounds seems never to have been discussed. In this instance, the p–T diagram shows, in addition to a single curve for the liquid–vapour equilibrium (Q–A–L), three curves for the solid–vapour and three for the solid–liquid equilibria. Two sub-cases, dependent on the different stability of the crystalline adduct, are shown in Figure 1(b and c): in 1(b) the decomposition temperature T_C is lower and in 1(c) higher than that of the pure enantiomer (T_A).

The solid–vapour curve intersects the liquid–vapour curve at point C; because of the congruent character of all the

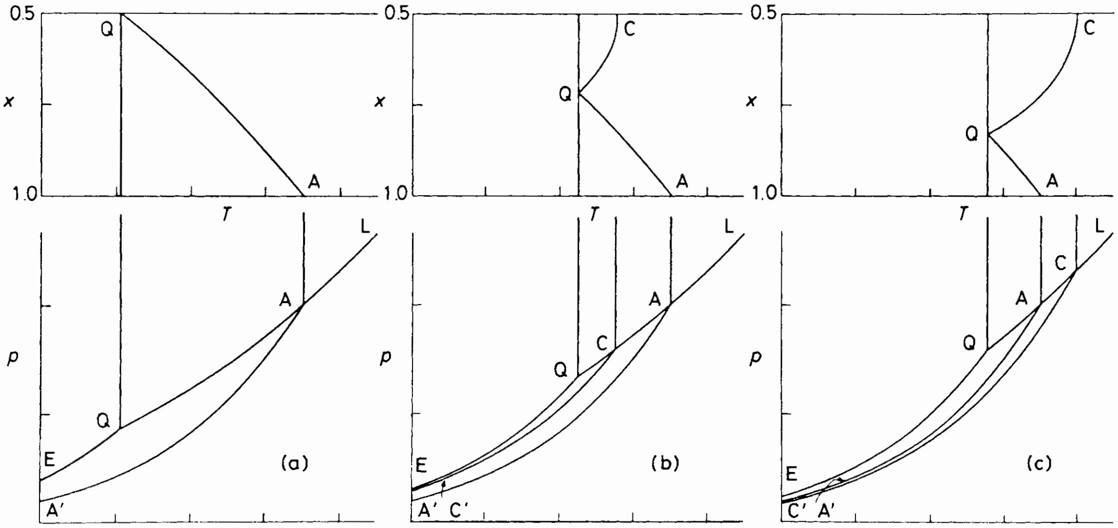

Figure 1. Calculated p–T diagrams of chiral compounds; in (a) the racemic mixture consists of a conglomerate, in (b) of a low stability racemic compound ($T_C < T_A$), and in (c) of a high stability racemic compound ($T_C > T_A$). For the sake of clarity the condensed phase diagrams are also reported.

involved phase transitions, the vapour pressure of the racemic compound can be calculated by using the Clausius–Clapeyron equation. The sublimation enthalpy is the sum of the decomposition enthalpy of the 1 : 1 adduct[6] (referred to one mole of chiral compound) and of the vaporization enthalpy of the liquid.

For partially resolved samples, the liquid–vapour curve extends below C (or A) and stops at point Q, a eutectic where four phases coexist: the crystalline racemic compound, the liquid, the vapour, and the excess of one enantiomer. Its composition corresponds to the intersection of the liquidus curves of the enantiomer and the racemic compound in the melting T–x diagram.[4]

The vapour pressure of the quadruple point and, generally speaking, that of crystalline mixtures of the racemic compound and an excess enantiomer at $T < T_Q$, is given by: $p = p_A + [p_C^2/(4p_A)]$, where p_A and p_C are the equilibrium pressures of the pure enantiomer and of the racemic adduct, respectively. It follows that the vapour pressure of partially resolved compounds (curve E–Q) cannot, in principle, be expressed by a simple equation, as in the cases of the pure enantiomers and of the racemic compound. Deviation from linearity of the $\ln p$ *vs.* $1/T$ diagram is most probably within experimental error; however the temperature coefficient cannot be interpreted in terms of heat of sublimation. In these systems, the vapour composition is no longer racemic and can be calculated according to the equation: $x = p_A^2/[p_A^2 + (p_C/2)^2]$ (x = mole fraction of one enantiomer).

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