Physical Chemistry of Organic Substances: Services, Development, and Research Work

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A review of selected highlights for services, development, and research work performed by the team “Applied Physical Chemistry” within the different and consecutive companies, namely J.R. Geigy, Ciba-Geigy, Novartis, and Solvias shall be outlined.
Certain general aspects will be discussed with respect to the style of the scientific development within such a team. Two extreme behaviours of a team are possible in relation to a permanent ongoing innovative development either as a dynamic process or as a conservation of the know-how at the scientific level of the status quo. The reasons, which cause a team to follow one or the other extreme – also a scientific development somewhere between the two extremes is possible – are not important, it is the fact, which counts. A high degree of enlargement and ongoing specialisation in the scientific know-how of a team affords different measures, favourable organisational conditions and qualities. One quality is above all the others necessary for any greater success of a team, namely the devotion of the members to their tasks.
Some selected examples of services, development and research work performed by the team “ Applied Physical Chemistry” will be outlined.
The first broader subject of the team was a development work within the applied chemical thermodynamics based on three instrumental methods, the Differential Scanning Calorimetry, the Thermogravimetry, and Isothermal Microcalorimetry. The subjects were related to the thermodynamic characterisation of crystalline, microcrystalline and amorphous substances, most in relation with the active ingredients of the J.R. Geigy AG. Subjects were elaborated such as eutectic purity, phase diagrams, liquid phases of crystalline powders, polymorphic forms, hydrates, solvates. At this time, practically no evaluation programs were available from manufacturers of instruments. It was a challenging task to elaborate such calculation procedures, which could be used for real industrial substances showing as an example in melting curves a variation of different effects such as coarse-grained crystals, solvents and water incorporated in the crystals, physical and chemical instabilities [1,2].
Improvements of the procedures for a determination of the enthalpy of fusion and the molar heat capacity of substances in crystalline and liquid form has been started with the development of the method for the eutectic purity determination. Enthalpy functions of different crystal modifications were elucidated and the question about the absolute stability of different crystal forms had been brought forward. Solubilities in several relevant liquid phases were measured as a service, especially also for drug substances with low values. The following questions had been formulated in 1973:

- How many crystal modifications are existing for a given drug substance?
- Which are the stability regions of polymorphic forms as a function of temperature and pressure?

The theoretical approach has been solved by thermodynamic functions for different polymorphs of a organic substance [3-7].
Another development work was started, namely the transpiration method in an inert gas flow (gas saturation method) used for the determination of the partial pressure of organic substances over a large temperature interval. We reached by this quasi-equilibrium method results of a high accuracy without using reference substances. Several additional vapour pressure methods were developed using mainly Thermogravimetry and DSC [8,9].
In the vast and risky project “Thermokinetics and KISA*” for the incineration of the dioxin-containing wastes from Seveso were all the members of the team for “Applied Physical Chemistry” involved. This project had been transferred to the team after I proposed measures to Anton Schaerli, plant director of Ciba-Geigy in Basel and to Dr. Bruno Böhlen, director of the Federal Office for Environmental Protection. The proposal contained measures for the reduction and the monitoring of emissions of dangerous substances during

the incineration and to preclude any hazard to the population and to the co-worker of Ciba-Geigy. The proposition of a reference substance, which could be decomposed in appropriate quantities in the hazardous waste incinerator, was of greatest importance to minimize the risk. This substance should have practically the same physicochemical properties as 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), however, revealing practically no toxicity. Additionally, the decomposition rates of TCDD and the selected reference material was measured in the laboratory over a broad temperature range using small sample masses to minimize the toxic risks. Test incinerations with the reference material using among others the KISA method, should reveal decomposition efficiencies for the different emission pathways, especially also for the flue gas. The decomposition of TCDD for a risk assessment could be estimated from the data of test incinerations with the reference material in relation of the decomposition rates and activation energies obtained in the laboratory experiments for the reference material and the TCDD. A decomposition efficiency for the TCDD in the waste from Seveso during the main incineration holding a mean temperature in the rotary furnace of 1530 ^{o}C was determined with respect to the emission stream through the flue gas much better than 0.999999 [10,11].

Over the years, the team "Applied Physical Chemistry" elaborated a great number of findings, some could be published. In addition the members of the team gave assistance for several inventions for the above named companies. Members of the team are indicated as inventors for about 10 patents. Furthermore, for practically all these patents we were the initiators and the researchers for the projects.

* KISA Short-interval trace analysis (Kurz-Intervall-Spuren-Analyse)

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