$\alpha = -0.4°$); HPLC (Chiralpak AS, *i*PrOH/hexane 3/7, 1 mL min^{-1}): $t_r = 5.1$ (1*S*,2*S*), 7.2 min (1*R*,2*R*).

Assignment of the absolute configuation: (1*S*,2*S*)-2-Amino-1,2-diphenylethanol was converted into an authentic sample of the 1*S*,2*S* enantiomer mentioned above by reaction with 2-bromopyrimidine.[12]

All other compounds were produced similarly. Regioisomers were usually separable by preparative TLC. It is advisable to keep the solvent polarity as high as possible; however, for some nonpolar olefins the addition of a small quantity of *n*-propanol was necessary to ensure the formation of homogeneous mixtures. A catalyst loading of 5% is sufficient for converting even heterocycles prone to electrophilic aromatic substitution. In most cases, however, it is possible to reduce the catalyst content to 1% without significant loss of *ee*; for example isopropyl cinnamate (Table 2, entry 1) gave 96% *ee* and 51% yield after 24 h. It is also usually possible to reduce the excess of the chlorinated salt of the heterocyclic amine to two equivalents.

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[10] For instance, 62% *ee* with Chloramine-T;[2a] 75% *ee* with Chloramine-M;[3] 94% *ee* with *N*-bromoacetamide;[4] 91% *ee* with *N*-halocarbarmate.[5]

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High-Resolution Calorimetry: New Perspectives for the Study of Phase Transitions**

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New developments in the area of microcalorimetry permit the thermal investigation of materials in sub-μg quantities.[1] The thermal investigation of masses in the picogram range is also of interest, for example, for the analysis of surfaces, and still represents a large experimental challenge. King and coworkers recently reported methods to perform the thermal analysis of adsorption phenomena,[2] but practical limits still exist that prevent these high-resolution methods, with a sensitivity in the nanojoule range, from having a wide application under simple laboratory conditions.

Presented herein is a calorimeter whose efficiency enables the thermal analysis of substances on the nano- and picogram scale and with a picojoule sensitivity by using simple experimental equipment. The calorimeter[3] is based on techniques well known in scanning probe microscopy and formed on a concept that was used to prove a surface reaction under high vacuum conditions.[4] We were able to quantify a solid–solid phase transition in *n*-alkanes in air. Only 7 pg of substance were needed. This corresponds to a released heat of a mere 500 pJ. The calorimeter furthermore has a time resolution of 0.5 ms, and dynamic effects can also be studied. This enables us to determine differences in the solid–solid phase transition of the *n*-alkanes while different phases are being formed. Differences in the phase dynamics of odd and even-numbered *n*-alkanes were also studied.

The essential item of the calorimeter (Figure 1) is a microfabricated composite cantilever in the form of a bimetallic

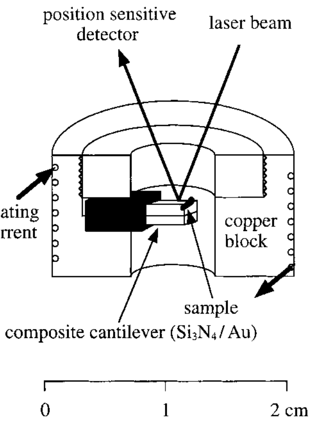

Figure 1. Schematic arrangement of the calorimeter. The heating block with the bimetallic cantilever are accommodated in a closed housing to avoid any disturbing air turbulence.

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strip. The deflection of the cantilever caused by a change in temperature is detected by using the optical deflection method.[3] The bimetallic cantilever is manually loaded with the *n*-alkane. The mass of the alkane is measured by analyzing the shift in the resonance frequency of the cantilever with a spectrum analyzer. This means that the bimetallic cantilever not only represents a very sensitive thermometer but also an exact balance for weighing small quantities of substance.[5]

The heating and cooling mode for a bimetallic cantilever carrying 15 ng tetracosane ($C_{24}H_{50}$) is given in Figures 2 a and 2 b, respectively. The deviations from the baseline arise from a solid–solid phase transition.[6] The phase transition from the crystalline into the rotator phase is shown in Figure 2 a. This phase transition occurs at a cantilever temperature of 47.5–48.0 °C. The formation of the crystalline phase from the rotator phase is given in Figure 2 b. The latter phase transition occurs at a remarkably lower cantilever temperature of 41.0 °C, which results from a supercooling of the rotator phase. It is clear that the rotator phase forms over a period of 3–4 s, while the formation of the crystalline phase from the supercooled rotator phase takes place within 40 ms. The temporal course differs too: the cantilever temperature is close to constant during the formation of the rotator phase as expected for a phase transition. The temperature of the cantilever rises abruptly and subsequently decreases smoothly during the growth of the crystalline phase from the supercooled rotator phase. Solid–solid phase transitions can exhibit remarkably different dynamics, depending on whether a rotator or a crystalline phase is formed. The differences in the phase transitions can be observed because the response time of the calorimeter is in the order of milliseconds.

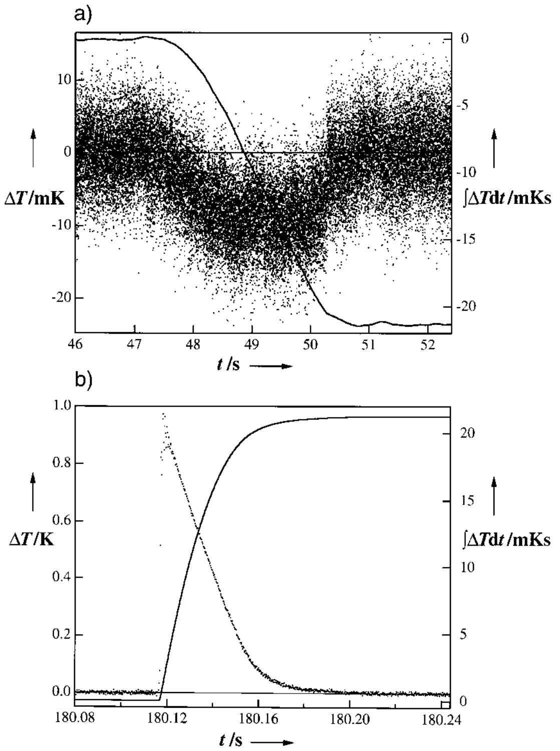

Figure 2. Section of the heating and cooling mode of a bimetallic cantilever that was loaded with a 15 ng tetracosane flake. The data represent the change in the cantilever temperature ΔT during the formation of the rotator phase (a) and the crystalline phase (b). The solid line corresponds to the time dependent integration $\int\Delta T\mathrm{d}t$ of the temperature change. The latter result is proportional to the consumed (a) or produced heat (b).

The energy that is released or consumed during the phase transitions can be quantified by an integration of the areas in Figures 2 a and 2 b. The solid line represents the integral. Both phase transitions yield identical areas and, therefore, similar heats, although the time dependence of the phase transitions varies significantly. The data of the processes can be reproduced with an error of 10 % for the rotator phase, and with an error of 5 % for the formation of the crystalline phase. In an independent second experiment, with an identically constructed cantilever, we found the apparatus constant of the calorimeter to be $6.5 \times 10^{-5}\,\mathrm{W\,K^{-1}}$. Therefore, the integrated areas in Figures 2 a and 2 b of $21 \times 10^{-3}\,\mathrm{K\,s}$ correspond to a transition heat of 1.36 μJ in both cases. With a sample mass of 15 ng this gives an enthalpy change for the particular tetracosane flake of 30.6 kJ mol^{-1} (literature value:[6] 31.3 kJ mol^{-1}). This demonstrates that the new calorimeter serves as a very sensitive tool for thermal analysis.

Besides tetracosane, we have also studied tricosane ($C_{23}H_{48}$) with the nanocalorimeter. Tricosane flakes of different masses showed the expected solid–solid phase transition. We again observed different kinetics during the formation of the rotator phase and the crystalline phase. On closer observation it was evident that tricosane and tetracosane form the crystalline phase in a different manner. While in the tricosane case even with a sample mass of more than 100 ng the increase of the cantilever temperature for the phase transition was limited to $\Delta T \approx 0.5$ K, tetracosane did not show this saturation effect for comparable sample masses ($\Delta T > 1.5$ K). It might be concluded from this observation that different kinetics exist for the formation of the crystalline phase in tetracosane (even number of carbon atoms) and in tricosane (odd number of carbon atoms).

For a sample loading of more than one nanogram the dynamics of the calorimeter is determined by the heat capacity of the sample mass, whereas in cases with a sample loading of significantly less than one nanogram, the dynamics of the calorimeter is only determined by the thermal properties of the bimetallic cantilever. The very small, but finite, mass of the cantilever represents the natural limit for the smallest detectable heat by the calorimeter, as well as for the time resolution of the experiment. To demonstrate the heat sensitivity and time resolution of the calorimeter, the bimetallic cantilever was loaded with a tricosane flake of 40 pg. The latter flake had a diameter of approximately 2–3 μm, and was still visible with an optical microscope. The resulting phase transition from the supercooled rotator phase is shown in Figure 3. The change in the cantilever temperature caused by the phase transition is clearly detected. The area under the peak of the first data set corresponds to a heat of 3.1 nJ or an enthalpy of formation of 25 kJ mol^{-1}. This fits the literature data of 21.8 kJ mol^{-1} very well, especially if one considers that the error in weighing the sample in air amounts to 25 %. With such small masses it is impossible to differentiate the signal for the formation of the rotator phase, which has to be collected over a time of 3–4 s, from the noise.

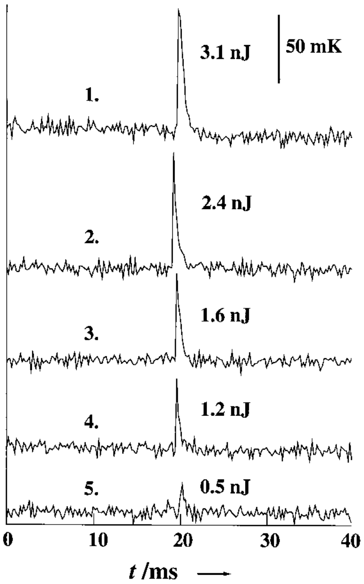

Figure 3. The recorded change in temperature of the cantilever ΔT, using the same 40 pg tricosane flake during the formation of the crystalline phase over five successive runs. The reduction of the transition heat is a result of the loss of substance by sublimation.

The phase transition from the supercooled rotator phase is well resolved because the crystalline phase forms rapidly. The area under the peak decreases smoothly on repeated runs as a result of partial sublimation of the sample. However, the formation of the crystalline phase is still detectable after five runs, and the area under the peak now corresponds to a transition heat of 500 pJ with a sample mass of about 7 pg. Although the amount of substance and the resulting heat of transition decreases with each run, the time constant of about 0.5 ms for the decrease of the cantilever temperature remains constant. In this case, the time constant is only defined by the intrinsic time constant of the bimetallic cantilever and not by the sample mass. The dynamics of phase transitions that are faster than 0.5 ms can, therefore, not be studied with this particular cantilever.

Besides analyzing phase transitions in solids, we have used an identically constructed calorimeter that was suitable for the application under high vacuum conditions for the thermal analysis of small metallic clusters in the gas phase.[7] So far, the calorimeter is limited to the thermal analyses of solids or reactions on solids. Future work will be focused on the fabrication of bimetallic cantilevers with integrated moulds for storing liquids and then carrying out thermal analysis. In fact, the thermal analysis can only be performed over an interval of approximately $\Delta T \approx 50\,^\circ\mathrm{C}$, but we hope to surpass this limit by the application of modified sensors. Samples in the nanogram range have already been analyzed thermogravimetrically up to 300 °C with piezo-resistive cantilevers.[8] In addition, special true differential experiments will rise the heat sensitivity. This also will enable the study of phase transitions over an expanded time scale.

Experimental Section

The calorimeter is schematically shown in Figure 1. Tetracosane and tricosane are commercially available (Fluka, p.a., purity $\geq 99.5\,\%$). The composite cantilevers can be obtained from Park Scientific.[9] The bimetallic cantilever is coated with a 50 nm gold layer on a 550 nm Si_3N_4 base. The cantilever was typically 200 µm long and 18 µm wide. The alkane flakes were placed manually on the cantilever. The adhesion of the alkane flake was monitored with an optical microscope. The flake must be put on the free side of the cantilever, otherwise an exact determination of the flake's mass with the aid of the spectrum analyzer becomes impossible. Next, the loaded cantilever was placed in the heater, and finally it was checked with the optical microscope that the laser beam had focused on the free gold-coated end of the cantilever. The reflected laser beam is directed by a mirror onto the position-sensitive detector. The copper block is heated at 2–3 W (this results in a heating rate of approximately 0.02 $\mathrm{K\,s^{-1}}$). The signal of the heater's thermocouple and the deflection of the bimetallic cantilever are recorded in parallel with 5000 data points per second. The small dimensions of the cantilevers allow fast thermal equilibration of the cantilever and the copper block. Therefore, the recorded heating block temperature equals the cantilever's temperature. The apparatus constant of the calorimeter is determined in an independent run with an identically constructed bimetallic cantilever. The calculation of absolute values for the transition heat at the phase transitions can now be carried out by using the temperature changes of the cantilever.

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