Gas Chromatography Problem Solving and Troubleshooting

Question

The results of a *N*,*N*-dimethylformamide (DMF) purity analysis performed in my lab is different than the results obtained in another lab. We are using identical capillary GC methods and techniques, but the DMF purity differs by about 5% for the same DMF sample. Each lab could consistently reproduce their results. In addition, the DMF peak is not symmetrical and all attempts to correct this problem have failed. What is the cause of the purity difference and asymmetric DMF peak? Which purity result is correct?

Answer

The capillary GC analysis of high-purity solvents requires specific GC conditions and a few compromises. In order to detect very low level impurities in a high-purity sample, a sufficient quantity of the sample has to be injected into the column. This results in a very large amount of the primary compound entering the column. Column, injector, and detector constraints occur because of the presence of both extremely high and low level compounds in the same sample.

Probably the most overlooked GC parameter for high-purity analysis is detector range. With a few exceptions, detector response or output is proportional to the amount of compound eluting from the column. The detector output is plotted versus time, which results in the familiar chromatogram. The area or height of each peak is calculated by the data system. Most detectors have a linear response over an amount range. For example, if the compound amount increases by two, the peak area or height also increases by a factor of two, as long as the range of the detector is not exceeded. Detectors have a maximum output signal that is not surpassed even if the compound is present in extremely high amounts. The output signal will remain at this sample maximum value until enough of the compound has eluted from the column. Exceeding a detector's output range results in flat-top or square peaks. An example is shown in Figure 1A. Peak areas or heights for out-of-range peaks can not be accurately calculated. While increasing the amount of an out-of-range compound results in larger peak area or height, they are no longer proportional with the sample amount. Relative peak areas or heights become skewed when one or more of the peaks are out of range. Sample purity can no longer be accurately calculated by comparing individual peak areas with the total peak area.

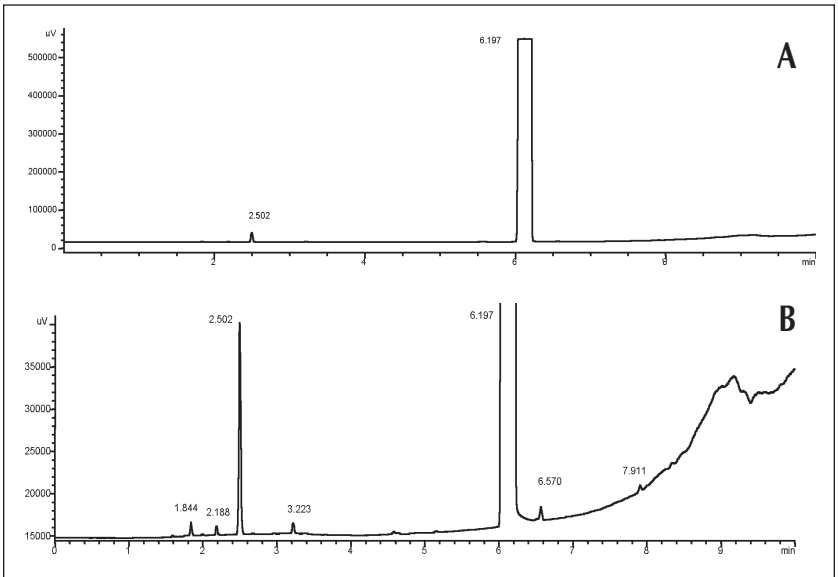

Figure 1. DMF chromatogram using a detector range of 0 at full scale (A) and reduced scale (B). The chromatographic conditions were a DB-WAX column (30-m × 0.53-mm i.d., 1.0 µm), split injector at 250°C and split ratio of 1:5, FID detector at 320°C, helium as the carrier gas at 31 cm/s, and a column temperature program of 70°C for 1 min (70–250°C at 20°/min).

The chromatogram in Figure 1 was obtained using a detector range of 0. A range of 0 is the default or typical value for most GC systems, and this range is suitable for most capillary GC analyses. A flat-top

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Dean Rood
Associate Editor

peak is obtained when the detector range is exceeded. Injecting a smaller sample amount, using a very high split ratio, or diluting the sample with another solvent are not viable options because the low level impurities will be below the detection limit of the method (these options also create other problems). The detector's maximum output signal can be increased by increasing the detector range value. Figure 2 shows the chromatogram obtained using a range of 6 for the exact same sample and GC conditions as in Figure 1. The peak using a range of 6 is now onscale without a flat top. An accurate peak area can now be obtained. Table I shows the data obtained using a detector range of 0 and 6. The purity results (peak %) for the two analyses are noticeably different. A new bottle of DMF used in this example reported purity of 99.9%. The purity obtained using a detector range of 6 is much closer to the value reported by the DMF supplier. Assuming the DMF sample is not contaminated, the +99.9% result is probably the more accurate analysis value.

Increasing detector range also decreases detector sensitivity. This is evident for the chromatograms in Figures 1B and 2B. The peaks in Figure 1B (range = 0) are larger, but the background is also increased. The relative peak percent of the peak at 7.911 min is calculated to be 3.798% for the detector range of 0. This value appears to be too high when visually comparing the relative peak sizes in the chromatogram. The sloping or noisy baseline is probably contributing to an integration error, which affects the peak-area and relative-area percent accuracy. Even though the sensitivity is lower at a range of 6 (Figure 2B), the small peaks are large enough to be easily detected and properly integrated. The more reasonable result at a detector range of 6 is caused by the onscale DMF peak and the more accurate integration of the small peaks.

Table I. Integration Data for Figures 1 and 2

Range 0

Retention time	Area	Symmetry	Area %
1.844	5281.97	1.508	0.080
2.188	4507.76	1.385	0.069
2.502	49,864.96	1.017	0.760
3.223	5701.30	1.037	0.087
6.197	6,228,946.50	5.810	94.887
6.570	20,976.26	1.800	0.320
7.911	249,311.27	22.467	3.798

Range 6

Retention time	Area	Symmetry	Area %
1.842	41.50	0.829	0.002
2.186	29.53	0.847	0.001
2.499	785.53	0.840	0.032
3.222	40.36	0.901	0.002
6.166	2,482,055.25	2.031	99.961
6.570	49.66	0.954	0.002
7.910	23.08	1.031	0.001

The DMF is present at a very high level (> 99.9%). Even with a very small injection volume, the amount entering the capillary column significantly exceeds the column capacity and an overloaded peak is obtained. Overloaded peaks have a pronounced slope or leading edge. The peak in Figure 2A is a good example of an overloaded peak. Trying to obtain a symmetry value between 0.9 and 1.1 for an overloaded peak is a futile exercise. To minimize the severity of the peak overload, wide-diameter and thick-film capillary columns are often used. Sample capacity increases as capillary column diameter and film thickness increase. Though a smaller diameter and thinner film column can be used, it will become overloaded at a much lower sample level. One benefit of using the higher detector range is the better symmetry value (Table I).

It is assumed that the detector has equal response for every sample compound when calculating sample purity using relative peak areas. Although this assumption is incorrect, the unequal detector response is usually ignored because correction factors can be difficult to calculate and often do not significantly change the results. The amount of error is dependent on the specific type of detector. Because the same sample and method was used in both labs, it is very unlikely that the purity analysis difference is caused by unequal response-factor issues.

The different purity results obtained between the two labs are probably related to the detector ranges being used. If one of the labs is using a detector range that is too low and out-of-range peaks are obtained, incorrect peak areas are probably being reported, which negatively affects the purity results. Obtaining ideal symmetry for an overloaded peak is an unrealistic expectation, and attempts to improve the symmetry will not work.

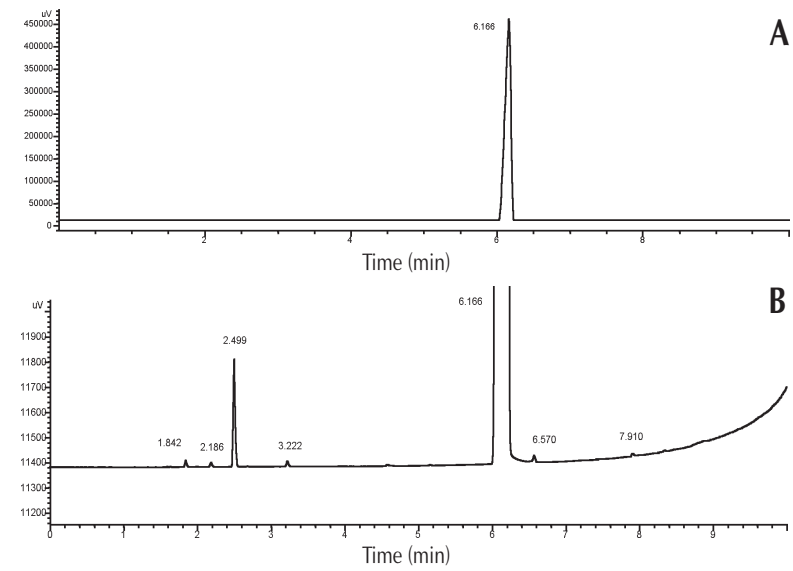

Figure 2. DMF chromatogram using a detector range of 6 and at full scale (A) and reduced scale (B). The chromatographic conditions were the same as for Figure 1.