## Some observations on quantitation in temperature programmed gas chromatography

The possibilities of quantitative analysis by gas chromatography are well known and have been described often in the literature and in text books. Reports on the application of quantitative gas chromatography to a specific problem are not, however, so frequent and very little can be found in the literature on the quantitative aspects of programmed gas chromatography.

In this paper the use is discussed of gas chromatography to investigate the Grignard addition reaction. In this investigation the relative reactivity of phenylmagnesium bromide towards acetophenone and derivatives was measured[1] using temperature programmed gas chromatography.

Equimolecular amounts of acetophenone and of a series of substituted acetophenones were allowed to react with an insufficient amount of phenylmagnesium bromide in diethyl ether and with diphenyl ether as internal standard.

By estimation of the surface of the gas chromatographic peaks of the recovered ketones, in relation to the surface of the diphenyl ether peak, the ratio of the reactivities is obtained. The same ratio can be determined by gas chromatographic determination of the amounts of reaction products. Comparison of the results obtained in the two ways showed excellent agreement and a Hammett plot was obtained with $\rho = 0.415$. The composition of the reaction mixture was rather complex and had a large boiling range.

Each mixture contained acetophenone (b.p. 202°), the acetophenone derivative (b.p. 200–310°), the internal standard diphenyl ether (b.p. 259°), the addition product of the acetophenone derivative with phenylmagnesium bromide (b.p. 250–400°), the addition product of acetophenone with phenylmagnesium bromide, diphenyl-methyl-carbinol (b.p. 260°), by-products of the Grignard reaction, *e.g.* phenol (b.p. 182°), methyl-phenyl-carbinol (b.p. 202–204°), biphenyl (b.p. 255°), and of course solvents such as ether and benzene. The by-products were identified after their separation from the reaction mixture by preparative gas chromatography (Aerograph 700).

The wide boiling range of the mixtures demands temperature programmed gas chromatography.

Separations in this way are perfectly possible and an advantage of the programming is that all peaks have nearly the same shape with sharp slopes showing little or no tailing. This is important for the ball and disc integrator which was used for integration. In isothermal chromatography the conditions can easily be kept constant during a run and differences between several analyses are eliminated by using an internal standard. With programmation the gas rate changes easily because of the increase of gas viscosity with temperature and although this could be standardised it should preferably be independent of starting temperatures and programming rates. This condition was fulfilled using an apparatus consisting of a dual column Aerograph 350-B (Wilkens Instruments) with thermal conductivity detectors in a separate oven, Moore differential flow controllers and needle valves. These allow a large pressure differential to be applied at the column inlet and are indeed necessary to obtain a constant gas flow through the detector cell regardless of programming rate or temperature. With three component mixtures it was found under these conditions that

the ratio of the peak areas was the same when programming from 40° onwards at 4°/min or when starting at 60° with a 6°/min heating programme.

Even without pressure drop at the column inlets and thus with a variable gas rate, reproducibility can be very good. This is shown in Table I, obtained for aceto-

TABLE I

| *No. of analysis* | *Substance* | *Temperature of emergence (C)* | *Relative surface* | *Gas flow rate* |
|---|---|---|---|---|
| 1 | Acetophenone | 190 | 0.6757 | 11.5 |
| | Diphenyl ether | 233 | 1 | 13.0 |
| | Acetonaphthone | 253 | 1.0434 | 13.8 |
| 2 | Acetophenone | 192 | 0.6863 | 11.5 |
| | Diphenyl ether | 234 | 1 | 13.0 |
| | Acetonaphthone | 253 | 1.0354 | 13.8–14.0 |
| 3 | Acetophenone | 191 | 0.6787 | 11.4 |
| | Diphenyl ether | 234 | 1 | 13.0 |
| | Acetonaphthone | 253 | 1.0505 | 13.8–14.0 |

phenone, diphenyl ether and acetonaphthone with a programme rate of 8°/min and a starting temperature of 170°. The gas flow is given as time in seconds for 10 ml. In general, however, instrument stability is much better with a pressure drop at the column inlets.

The high temperature necessary for the analyses restricted the choice of stationary phase. The use of combined columns with SE30 and Apiezon L made possible the analysis of all the mixtures. SE30 separates diphenyl ether and biphenyl but separation of acetophenone and the carbinols is not so good. Apiezon L gives excellent separation of the acetophenones and the carbinols, but diphenyl ether and biphenyl are not separated. Analysis on SE30 then gives the correction necessary in the analyses on Apiezon L. Quantitation of the results was obtained with a disc integrator. The accuracy of this device is excellent and was in our case $\pm$ 0.15 %. The analysis of each mixture was repeated until at least 9 values for the relative reactivity were obtained. The maximum deviation between the values was *ca.* 5 % and the deviation of the mean value from the Hammett plot was at most 1 %. To obtain this accuracy, the baseline on the chromatogram has to remain constant to 0.1 % of the total deflection, otherwise the integrated peak surfaces are valueless. This can be obtained on a not too sensitive attenuation setting ( 4 $\times$ or 8 $\times$) when the stationary phase is stable and when no decomposition occurs.

Frequently, however, after the emergence of a peak, the baseline did not come back to absolute zero, but showed a shift of 0–2 mm. The reason for this is unknown. Although hardly noticeable at first glance this had to be corrected for the quantitation by manual setting of the instrument so that the chromatograms needed constant attention. An interesting point about possible decomposition is that diphenylmethyl-carbinol was destroyed on SE30 but not on Apiezon L although all other conditions were maintained identical. After prolonged use the Apiezon L columns also destroyed this alcohol.

Because of the high cost of helium in Europe the possible use of hydrogen as carrier gas for quantitative work was investigated. Curiously enough the accuracy of the results was not as good as with helium, the deviation on relative areas being about three times as great. It was at first thought that a possible reaction on the heated wires (hydrogenation) was responsible. However, the relative surfaces of a mixture of toluene and *trans/cis*-decalin was the same using helium or hydrogen. This makes hydrogenation or dehydrogenation on the detector wires improbable. The reason for the better results with helium than with hydrogen is unknown to us. The stability of the instrument seems to be better with helium than with hydrogen. For very precise quantitative work with katharometer detection, therefore, it seems that hydrogen is less suitable than helium.

An example of a chromatogram is shown in Fig. 1a, obtained with a 2 m column filled with 15 % SE30 on celite. The programming was 6°/min and the starting tem-

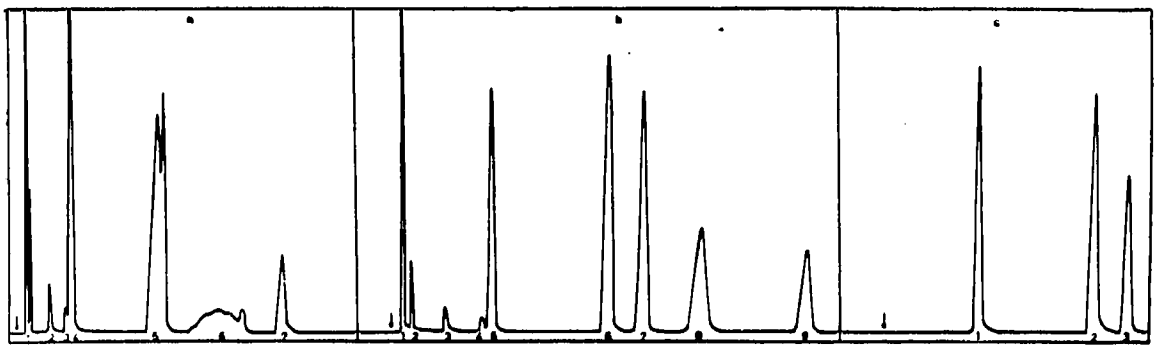

Fig. 1. Separation by temperature programmed gas chromatography of a competitive Grignard reaction mixture as explained in the text (Aerograph 350-B).

perature 136°. The order of emergence is ether and benzene (1), phenol (2), methyl-phenyl-carbinol (3), acetophenone (4), 4-methoxyacetophenone, biphenyl and diphenyl ether in a composite peak (5), methyl-diphenyl-carbinol with decomposition (6) and 4-methoxyphenyl-methylphenyl carbinol (7). The chromatogram of Fig. 1b shows the same separation on a 2 m column with 15 % Apiezon L on celite. The same operational conditions ware maintained. The order of emergence is ether (1), benzene (2), phenol (3), methyl-phenyl-carbinol (4), acetophenone (5), 4-methoxyacetophenone (6), biphenyl and diphenyl ether (7), methyl-diphenyl-carbinol (8) and 4-methoxy-phenyl-methylphenyl-carbinol (9). The chromatogram of Fig. 1c is obtained on the same column and under the same conditions as Fig. 1b and shows the separation of an equimolecular mixture of acetophenone (1), 4-methoxyacetophenone (2) and the internal standard diphenyl ether (3) to which the Grignard reagent was added. From the surfaces relative to the diphenyl ether peak in Fig. 1b and 1c the relative reactivity of acetophenone and 4-methoxyacetophenone can be calculated.

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1 M. ANTEUNIS AND J. VAN SCHOOTE, *Bull. Soc. Chim. Belg.*, 72 (1963) 776.

Received July 13th, 1964