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## Note

# Gas chromatographic separation of 2,6-dimethylpyridine and its chloro derivatives

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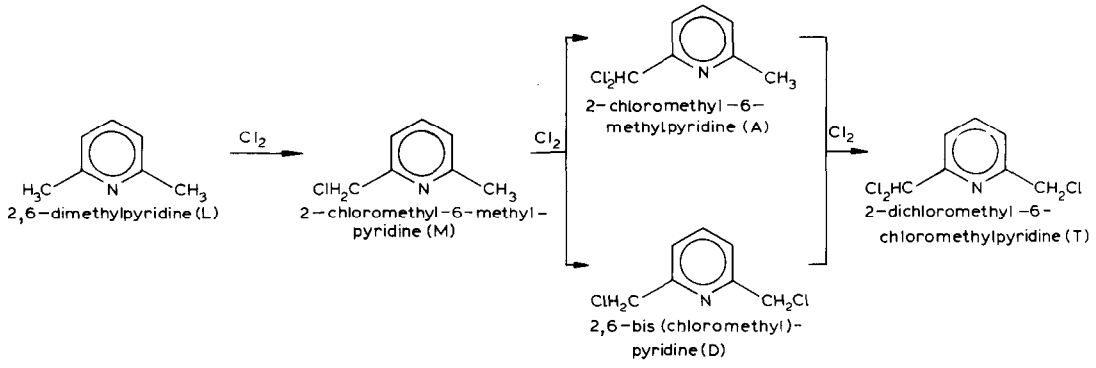
2,6-Bis(chloromethyl)pyridine, a pharmaceutical intermediate, is prepared by free radical chlorination of 2,6-dimethylpyridine (2,6-lutidine)[1]. Owing to parallel and consecutive side-reactions there are several components in the reaction mixture:




As it was necessary to follow the course of the reaction, we developed an optimized, rapid gas chromatographic (GC) separation to quantify lutidine and its chloro derivatives.

The window diagrams proposed by Purnell and co-workers[2–8] permit the optimization of the composition of mixed GC phases resulting in the best possible separation of all the components of the sample.

The separation of 2,6-lutidine and the solvent proved difficult, because the capacity factor of 2,6-lutidine is small and the excess of solvent is large. Therefore, the first task was the complete separation of these two compounds. As a second optimization criterion, the retention time of the last eluted component (T) had to be kept at a minimum.

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## EXPERIMENTAL

### *Apparatus*

Experiments were carried out with a Sigma 2 gas chromatograph (Perkin-Elmer, Norwalk, CT, U.S.A.), equipped with a flame ionization detector, a Minigrator integrator (Spectra-Physics, Santa Anna, CA, U.S.A. and a Model 6 recorder (Perkin-Elmer).

### *Column*

Columns were packed with 100–120-mesh Chromosorb W AW DMCS, coated with 5% (w/w) of stationary phase. Pyrex glass columns (2 m × 2 mm I.D.) were used. The following stationary phases were selected to represent the fundamental intermolecular interactions: OV-101, dispersion; OV-25, induction; OV-275, orientation, electron donor; OV-330, orientation, hydrogen bonding.

## RESULTS AND DISCUSSION

Using the most polar of the four stationary phases selected, the lowest temperature at which the extent of tailing was acceptable was determined. Using this temperature (120°C), the optimum gas velocity leading to the minimum plate height was determined (26 ml/min).

The chromatograms of all the lutidine derivatives were obtained on all four columns using identical separation conditions (injector, detector and oven temperature, carrier gas velocity, phase loading, support, column length and efficiency). The distribution coefficients used in the window diagrams were calculated from the retention data.

The window diagrams of the non-polar–selective and selective–selective phase pairs were constructed from the measured values. The elution order was L, M, A, D and T on each column. Only the values of the immediate neighbours are shown in the window diagrams because the separation of the other components is easy. From the window diagrams it is apparent[9] that the highest selectivity for the benzene–lutidine pair is obtained on pure OV-330 stationary phase. The retention time of the last component, T, however, is almost twice as large on OV-330 as on OV-101, while the benzene–lutidine selectivity is only slightly lower on OV-101 than on OV-330. The window diagrams revealed that the use of mixed stationary phases does not offer any advantage in this instance. the selectivities offered by the windows were either smaller than on OV-101 or, if comparable, the retention time of T was much higher.

It was concluded that pure OV-101 is optimal for the separation of benzene, lutidine and its chloro derivatives. Therefore, the separation temperature for the OV-101 phase was optimized using the window diagram method[10]. The other temperatures used for the optimization were 100 and 130°C. The window diagram obtained is shown in Fig. 1. The separation selectivity for the benzene–lutidine pair (LB) increases only slightly as the temperature is lowered, but the retention time of the last eluted component increases rapidly. There is a window at 115°C, where the selectivity is optimal.

The optimal separation conditions are as follows: stationary phase, 5% (w/w) OV-101; column temperature, 115°C, isothermal; carrier gas (nitrogen) velocity, 26

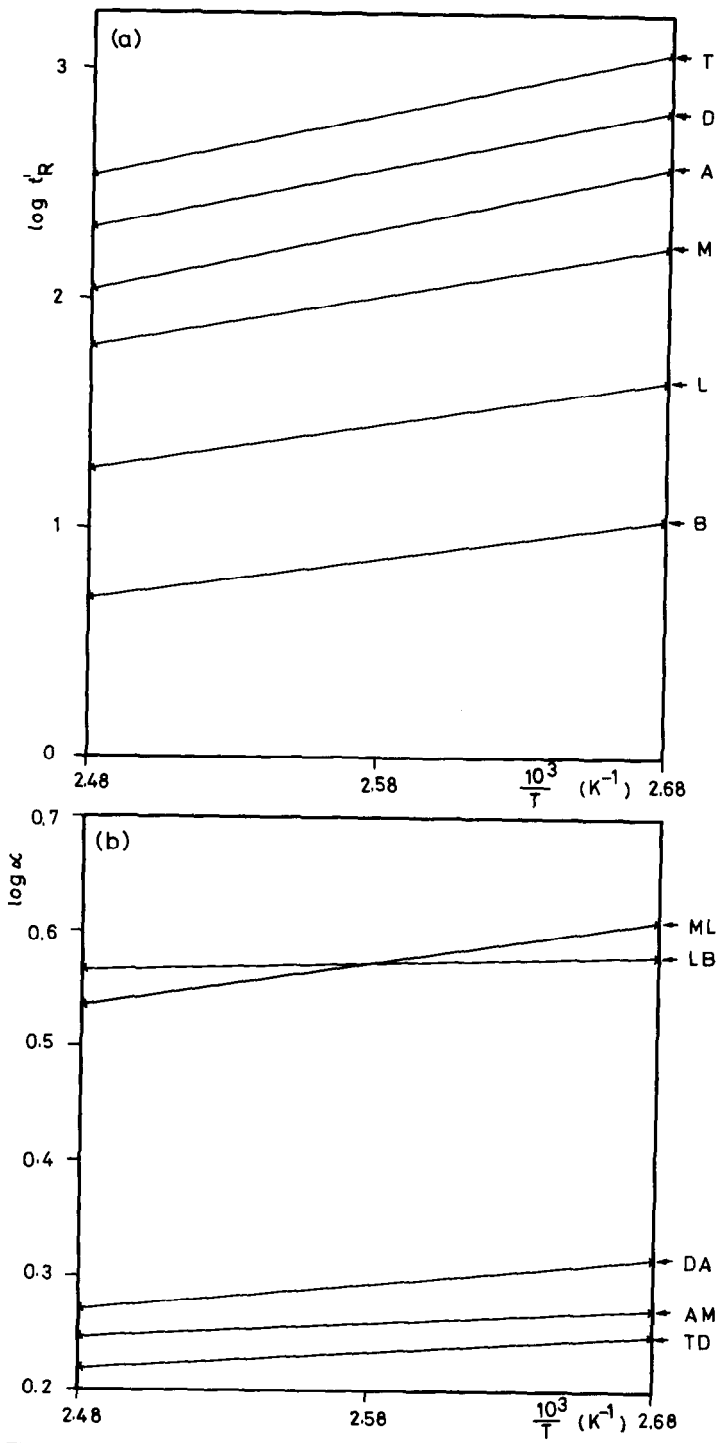


Fig. 1. (a) Log $t'_R$ versus $10^3/T$ diagram for the six components and (b) the window diagram constructed from it (B = benzene).

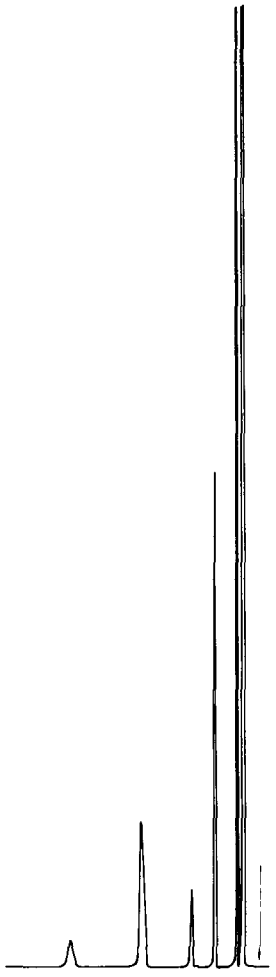

Fig. 2. GC separation of 2,6-lutidine and its chloro derivatives on an OV-101 column under optimized conditions. Injector temperature, 190°C; column temperature, 115°C; detector temperature, 200°C; carrier gas velocity, 26 ml/min.

ml/min; detector temperature, 200°C; and injector temperature, 190°C. The chromatogram obtained using these conditions is shown in Fig. 2. It can be seen that all six components are well separated and the analysis time is sufficiently short.

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