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Note

High-performance liquid chromatographic separation of the intermediate products in the synthesis of trimethylolpropane

LUCIANO CAIRATI, MARCO CANNIZZARO, ANDREA COMINI and GIUSEPPINA GATTI
S.I.S.A.S., Largo Corsia dei Servi 3, Milano (Italy)
and
PAOLA VITA-FINZI*
Istituto di Chimica Organica dell'Università degli Studi, Via Taramelli 10, 27100 Pavia (Italy)
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Industrial synthesis of trimethylolpropane (TMP) can be carried out by condensation of *n*-butyraldehyde with formaldehyde followed by catalytic hydrogenation of the reaction products.

During the synthesis it is important to be able to control the composition of the condensation mixture before hydrogenation by a fast analytical method. Since most of the components are quite unstable and of low volatility, thin-layer chromatography (TLC) and high-performance liquid chromatography (HPLC) seemed to be the most suitable methods for this purpose, and here we report the method we worked out.

For a preliminary TLC analysis, silica gel or RP-8 bonded silica gel plates were used. For separation of the intermediates in the TMP synthesis by HPLC three different columns were employed: LiChrosorb RP-2 (10 μm; Merck); RP-8 (10 μm; Perkin-Elmer); and μBondapak CN (Waters). In all cases, mixtures of the following solvents were used as the mobile phase: water, tetrahydrofuran (THF), acetonitrile and methanol. The best results were obtained on LiChrosorb RP-2 by elution with water–methanol.

In order to confirm the structure of the components, preparative HPLC was carried out on a preparative Lobar RP-8 (Merck) column by elution with water–methanol.

EXPERIMENTAL

Apparatus

A Perkin-Elmer Series 3 liquid chromatograph equipped with a microprocessor, a Rheodyne 7105 injection valve and a Perkin-Elmer 023 recorder was used. The detector was a DuPont refractive index device.

Columns

LiChrosorb RP-2 (10-μm particles) Merck, 25 cm × 6.5 mm; Lobar LiChroprep RP-8 (40–63 μm particles) Merck, 31 cm × 25 mm.

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Reagents and standards

Mixtures of the following solvents were used as mobile phases: glass-distilled water filtered on a 0.45-μm Millipore filter; methanol for chromatography (LiChrosolv; Merck). Degassing was accomplished under vacuum just before the analysis.

TMP used as standard was purchased from Fluka, *n*-butyraldehyde and formaldehyde from Carlo Erba, α-ethylacrolein was prepared following the literature data[1].

TLC analysis were performed on Kieselgel 60 F_{254} plates (0.25 mm, Merck), and on HPTLC RP-8 F_{254} plates (Merck).

Conditions and procedures

TLC plates were eluted with chloroform–methanol (9:1); HPTLC plates with water–methanol (7:3). In both cases spots were visualized by exposure to iodine vapours.

HPLC of the reaction mixtures of the TMP synthesis was performed as follows: LiChrosorb RP-2, elution with water–methanol (70:30), flow-rate 1 ml/min; the sample (1 μl) was injected without dilution. Quantitative analysis was carried out by injection of 10 μl after diluting the crude mixture 1:9.

For preparative HPLC the best separation was afforded using water–methanol (80:20) as the mobile phase with a flow-rate of 3 ml/min.

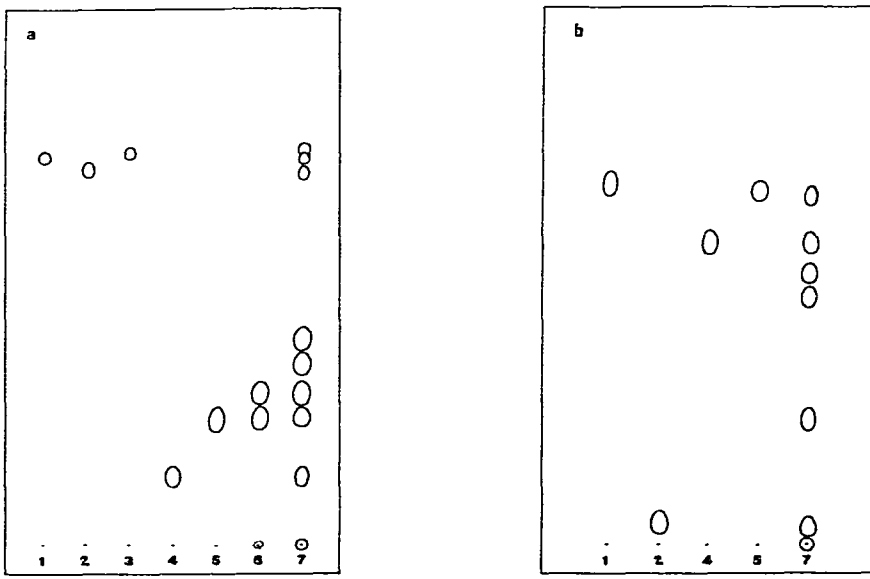

Fig. 1. TLC analysis of a TMP synthesis solution. a, Kieselgel 60 F_{254} plates, eluent chloroform–methanol (9:1); spots visualized by exposure to iodine vapours. 1 = Formaldehyde; 2 = *n*-butyraldehyde; 3 = α-ethylacrolein; 4 = TMP; 5 = 2,2-dihydroxymethylbutanal; 6 = mixture of spot 5 and its oligomeric compound and formates; 7 = reaction mixture containing compounds 1–6 and two formals. b, HPTLC RP-8 F_{254} plates, eluent water–methanol (7:3); spots visualized by exposure to iodine vapours. 1 = Formaldehyde; 2 = *n*-butyraldehyde; 4 = TMP; 5 = 2,2-dihydroxymethylbutanal; 7 = reaction mixture containing from the higher R_F the following compounds: 2,2-dihydroxymethylbutanal, TMP, two formals, the oligomeric compounds of 2,2-dihydroxymethylbutanal, *n*-butyraldehyde and α-ethylacrolein.

RESULTS AND DISCUSSION

In previous work[2] components of the crude aldol condensation for the synthesis of TMP were identified as *n*-butyraldehyde, formaldehyde, formates, TMP, α-ethylacrolein, 2,2-dihydroxymethylbutanal, its oligomeric compounds and two formals.

By TLC (Fig. 1a and b) some of the aldol reaction products could be identified and conditions for HPLC could be determined by HPTLC.

As described above, three different columns and conditions were employed for the HPLC analysis but the μBondapak CN column was discarded because of the tailed peaks and the RP-8 column because the retention times of the components were too high and some of the products were not separated, *e.g.*, α-ethylacrolein and the oligomeric 2,2-dihydroxymethylbutanal. A LiChrosorb RP-2 column gave the best results because all the components were well separated in a relatively short time.

By comparison of the retention time with authentic samples we could establish the elution order: formate, formaldehyde, TMP, 2,2-dihydroxymethylbutanal, formal, formal, oligomeric 2,2-dihydroxymethylbutanal, *n*-butyraldehyde and α-ethylacrolein.

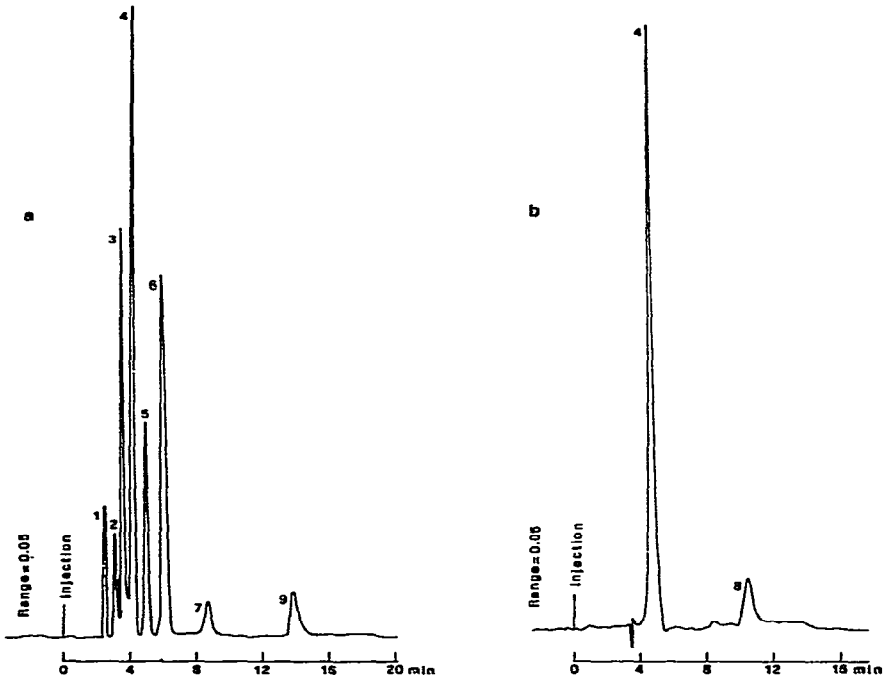

Fig. 2. a, HPLC separation of components in a TMP synthesis solution. Column: LiChrosorb RP-2 (10 μm) 25 cm × 6.5 mm. Mobile phase: water–methanol (70:30), 1 ml/min. Peaks: 1 = sodium formate; 2 = formaldehyde; 3 = TMP; 4 = 2,2-dihydroxymethylbutanal; 5 = formal I; 6 = formal II; 7 = *n*-butyraldehyde; 9 = α-ethylacrolein. No sample dilution, 1 μl injected. b, Sample of the preparative HPLC separation. Same conditions as in a. Peaks: 4 = 2,2-dihydroxymethylbutanal; 8 = oligomeric compound. Sample dilution 1:9, 10 μl injected.

Preparative HPLC was applicable for the separation of a pure sample of 2,2-dihydroxymethylbutanal which after a short time showed a second peak corresponding to the oligomeric compound indicating an equilibrium of the two products. Similarly, when the two formals were obtained in a pure form by preparative HPLC, they showed, also in a short time, peaks corresponding to formaldehyde and 2,2-dihydroxymethylbutanal.

In Fig. 2a we report the HPLC of a reaction mixture lacking the oligomeric 2,2-dihydroxymethylbutanal and in Fig. 2b the chromatogram of a sample of 2,2-dihydroxymethylbutanal collected by preparative HPLC but performed one day later. It also shows the presence of the oligomeric compound.

CONCLUSIONS

HPLC can be used as qualitative and quantitative control analysis of the composition of the intermediate aldol condensation mixture in the synthesis of TMP. The described method is very easy to perform and is suitable for routine analysis in industrial synthesis of TMP.

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REFERENCES

1 M. I. Farberov, G. S. Mirouov and M. A. Korshunov, *Zh. Prikl. Khim.*, 35 (1962) 2483.
2 L. Cairati, M. Cannizzaro, A. Comini, G. Gatti, I. Pasquon and P. Vita-Finzi, *Chim. Ind. (Milan)*, in press.