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Note

Separation of dichloro- and chlorofluorobenzophenone isomers by high-performance liquid chromatography

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A variety of chromatographic techniques has been used for the separation and characterization of benzophenones and related compounds. Vessman and co-workers¹⁻⁸ reported extensive work on the characteristics of benzophenones by gas-liquid chromatography (GLC) with electron-capture detection. Abou-Donia⁹ studied four liquid phases on Chromosorb W in combination with an electron-capture detector for the GLC analysis of 25 DDT-type compounds including 4,4'-dichlorobenzophenone and 4-chlorobenzophenone. Benzra¹⁰ separated mixtures of aromatic ketones at the sub-nanogram range by plasma chromatography. Reversed-phase high-performance liquid chromatography (RP-HPLC) with UV detection was used to separate and detect 2,4'- and 4,4'-dichlorobenzophenones, the degradation products of the corresponding 2,4'- and 4,4'-Dicofol¹¹. Chlorine-selective detection for liquid chromatography with a Coulson electrolytic conductivity detector (CEICD) showed high selectivity to organochlorine compounds relative to hydrocarbons, with a linear range of 10^5 . However, the CEICD/UV₂₅₄ response for dichlorobenzophenone was 0.01 thus favoring the UV detection¹².

Relatively little work has been published on the isomeric determination of dihalogenated benzophenones. Determination of the isomer ratios for compounds related to dichlorobenzophenone, di(chlorophenyl)methane and di(chlorophenyl)ethane by infrared, ¹H nuclear magnetic resonance and mass spectroscopy were found to be of a limited use¹³⁻¹⁷. Abraham *et al.*¹⁷ separated a mixture of dichlorobenzophenones by GLC. However, in our hands the 2,3'- and 2,4'-dichloroisomers were not completely resolved. Recently¹⁸ we reported the complete separation of 2,2'-, 2,3'- and 2,4'-dichlorobenzophenones by thin-layer chromatography (TLC). Both the GLC¹⁷ and TLC¹⁸ techniques require a long time for resolving the isomeric mixture.

The objective of this work was to find suitable HPLC conditions which allow the resolution of dichloro- and chlorofluorobenzophenones in a short time and the application of such a system in the routine identification of the various isomers.

EXPERIMENTAL

The system used for the HPLC work included a Waters Model 6000A pump (Waters Assoc., Milford, MA, U.S.A.). The detector was a Varian variable-wave-

length Vari-chrom unit (Varian, Palo Alto, CA, U.S.A.) operated at 254 nm and fitted with an 8- μ l flow cell. Data were collected with a Hewlett-Packard 1000 series 2117F computer (Hewlett-Packard, Palo Alto, CA, U.S.A.) at a sampling rate of 0.33 Hz. Post-run plots of the chromatograms were generated on a Hewlett-Packard Model HP-72215 plotter. A Rheodyne Model 70-10 liquid sampling valve (Rheodyne, Berkeley, CA, U.S.A.) with a 20- μ l sample loop was attached to a 25 \times 0.46 cm DuPont Zorbax[®]-ODS column. The column was maintained at room temperature. However, the column was wrapped with an insulating material to prevent large fluctuations in temperature. The mobile phase consisted of "Milli-Q" water-tetrahydrofuran (55:45). This solution was degassed and kept magnetically stirred. Because of the viscosity of the eluting solvent, a system equilibration time of about 30 min was required to reach a stable baseline. The mobile phase was pumped at a flow-rate of 1.0 ml/min through the column, producing a column head pressure of approximately 3000 p.s.i. The benzophenone standards were dissolved at a concentration of about 0.08 mg/ml of the eluting solvent. The isomers of interest were available from our Process Research Laboratory (see Acknowledgement).

RESULTS AND DISCUSSION

To the best of our knowledge this is the first HPLC system reported to the literature for the separation of dihalogenated benzophenones. The capacity ratios of the seven benzophenones of interest to us are given in Table I. For the monosubstituted rings (compounds 1-3) the order of increasing retention time follows the sequence: 2,2' < 2,3' < 2,4'. A similar trend was reported by Abraham *et al.*¹⁷ in the GLC work on dichlorobenzophenones. We found that in every case, the retention times of the chlorofluorobenzophenones were less than the corresponding dichlorobenzophenones. The 2,4-disubstituted ring (compound 4) showed the longest elution time. Fig. 1 shows the baseline resolution of the isomers.

TABLE I

CAPACITY RATIOS OF SOME DIHALOGENATED BENZOPHENONES

No.	Isomer	Capacity ratio
<i>Dichlorobenzophenones</i>		
1	2,2'	4.5
2	2,3'	6.6
3	2,4'	8.1
4	2,4	9.0
<i>Chlorofluorobenzophenones</i>		
5	2,2'	3.7
6	2,3'	5.3
7	2,4'	5.8

In conclusion, this HPLC system allowed us to separate the positional isomers of the chlorofluorobenzophenone series and the dichlorobenzophenone series in less than 16 min, thus assuring a rapid identification of the isomeric content per sample.

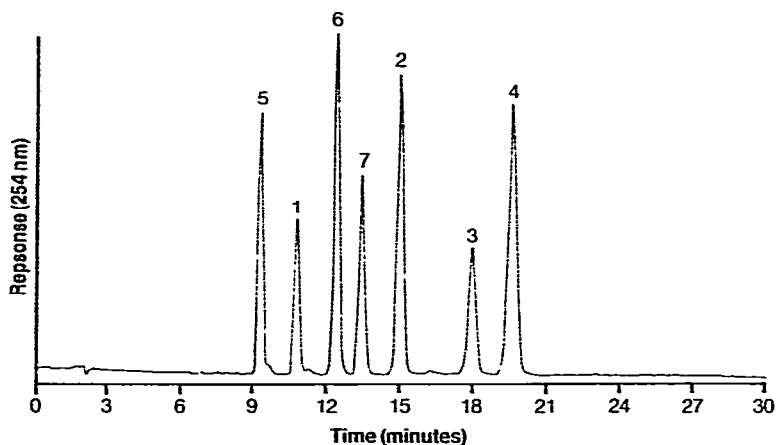


Fig. 1. HPLC of some dihalogenated benzophenones. Peak numbers correspond to Table I.

This isocratic HPLC procedure complements the TLC procedure reported before¹⁸. The detailed quantitation of the isomeric content and other related material in 2,4'-dichlorobenzophenone raw material will be the subject of another manuscript.

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