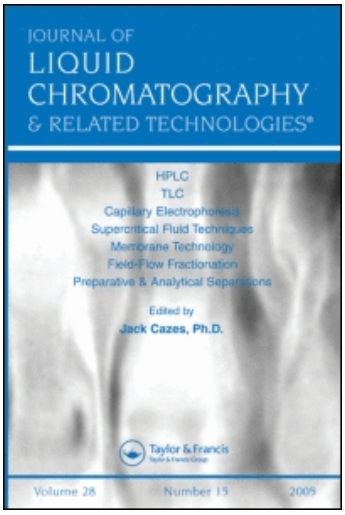

Journal of Liquid Chromatography & Related Technologies
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597273

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To cite this Article Smith, S. L. , Bishara, R. H. and Drummond, G. E.(1981) 'The Separation of Dichlorobenzophenone Isomers by Continuous Development and Reversed-Phase Thin Layer Chromatography', Journal of Liquid Chromatography & Related Technologies, 4: 12, 2205 — 2212
To link to this Article: DOI: 10.1080/01483918108066853
URL: http://dx.doi.org/10.1080/01483918108066853

JOURNAL OF LIQUID CHROMATOGRAPHY, 4(12), 2205-2212 (1981)

THE SEPARATION OF DICHLOROBENZOPHENONE ISOMERS BY CONTINUOUS DEVELOPMENT AND REVERSED-PHASE THIN-LAYER CHROMATOGRAPHY

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ABSTRACT

Two thin-layer chromatographic methods are described for 2,4'-dichlorobenzophenone with which 1% of the 2,2'- and 2,3'-isomers can be determined. Continuous thin-layer chromatography on silica gel and conventional reversed-phase thin-layer chromatography were found to be complementary techniques for the separation of the dichlorobenzophenone isomers.

INTRODUCTION

Dichlorinated benzophenones are intermediates in the synthesis of selected fungicides and other agricultural products. In the Friedel-Crafts synthesis for the preparation of these chemicals, small quantities of isomeric impurities are also produced. In our laboratory, the purity of 2,4'-dichlorobenzophenone must be controlled to prevent carry-over of isomeric impurities to the final product, a chemical fungicide.

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Relatively little has been published on the chromatographic separation of these benzophenones. Perhaps the most extensive work has been a gas-chromatographic procedure reported recently by Abraham et al. (1). However, because this procedure is time-consuming and the resolution is insufficient for the determination of minor isomeric impurities, the method is not readily adapted to a real-time control situation.

A variety of TLC systems have been used for the separation of halogenated aromatic compounds (2-6). Applications include the separation of polychlorinated biphenyls (3) and the separation of chlorinated insecticides (4). Tewari and Sharma (5) report the thin-layer chromatographic behavior of a number of chlorinated pesticides in 26 different solvent systems; several chromogenic reagents were investigated in this work. A review of pesticide analysis by TLC has been published by Sherma and Zweig (6).

Despite the widespread use of TLC in the analysis of halogenated fungicides, pesticides, and insecticides, there are few reports on the resolution of isomeric halogenated aromatics by thin-layer chromatography. In an early report, Fishbein (7) separated a number of halogenated derivatives of aniline and benzene using three separate systems. However, with the conditions investigated, the isomeric dichlorobenzenes were not separated.

In this work, simple TLC methods are described for 2,4'-dichlorobenzophenone with which 1% of the corresponding 2,2'- and 2,3'- isomers can be detected.

We had screened a variety of TLC systems according to a previously described procedure (8). Using conventional thin-layer chromatography (i.e., using ascending development in a closed, saturated chamber over a bed length of 15 cm), equal concentrations of the three isomers could be separated. Our original optimized TLC system consisted of silica gel TLC plates and

carbon tetrachloride/benzene (4:1) as the developing solvent. However, the 2,2'- and 2,3'- isomers could not be separated at a level less than 10% of the 2,4'- main component.

Approaches to enhance the resolution of compounds with similar Rf values in conventional TLC are well documented (9-12). These approaches include successive development over two dimensions (10), multiple development (11), and continuous development over the 20-cm plate (12). The first two techniques require repeated operator interaction. All three suffer from solute diffusion problems and, consequently, high detection limits. Perry (13) recently discussed the combination of continuous development TLC with short bed lengths. With this approach, the selectivity of nonpolar solvents can be utilized without excessive spot diffusion. Perry indicated that this form of continuous TLC might be most applicable to difficult separation problems. This technique was investigated for the separation of the dichlorinated benzophenones.

In the last few years, reversed-phase chromatography has been widely applied to the separation of positional isomers of relatively nonpolar compounds. Here, the possibility of utilizing reversed-phase TLC plates to resolve the isomers of dichlorobenzophenone is also reported.

EXPERIMENTAL

Silica gel 60 F_{254} TLC plates (EM Laboratories, Inc., Elmsford, N.Y. 10523), 20 cm x 5 cm with 0.25-mm-thick layer, were used for all of the continuous development TLC separations. A stock solution of the 2,3'- and 2,2'- dichlorobenzophenone isomers was prepared at a concentration of 2.8 mg/ml in methanol. Ten, five, and one percent solutions of these isomers in the presence of the 2,4'- dichlorobenzophenone were prepared from this solution. One-microliter aliquots were applied to the TLC plate.

The equipment needed to perform the continuous TLC with short beds was available commercially (Regis SB/CD TLC chamber, Regis Chemical Company, Morton Grove, Illinois 60053). However, for this work, a convenient screening chamber was designed which could accommodate up to six plates with variable bed lengths and choice of developing solvents.

A conventional TLC chamber (20.7 cm x 8.7 cm) was modified to accommodate continuous development and a variety of bed lengths (Figure 1). The glass chamber was cut to a height of 10.5 cm and fitted with a tight-fitting Teflon lid, 1.3-cm thick. Slits (5.1 mm x 2 mm) were machined 3.0 cm apart in the Teflon parallel to its width. The slits were the proper geometry to just allow insertion of the 5 x 20 cm plates without disruption of the silica gel layer. Glass solvent reservoirs, 6 cm x 2 cm x 10 cm in height, were placed inside the chamber and made a tight seal with the Teflon lid. During development, the chamber was placed in a laboratory hood which had an air flow of approximately 200 ft/min. Under these conditions, the developing solvent traveled up the TLC plate and evaporated when it reached the top

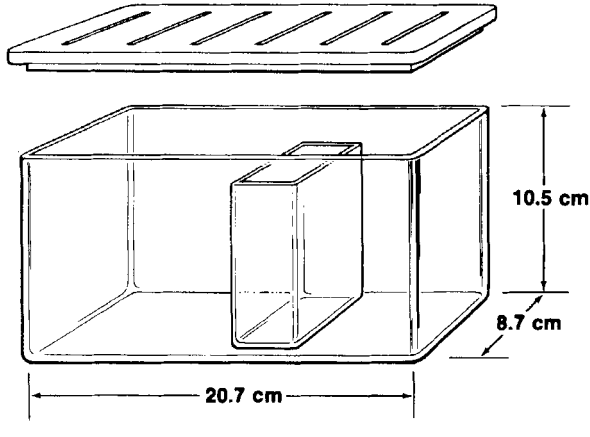

Figure 1: Continuous development TLC chamber.

of the Teflon cover. Bed lengths were varied by changing the depth of solvent in the individual reservoirs. For any depth, the samples were applied 5 mm above the solvent line.

This experimental arrangement proved to be a very efficient and economical system for continuous thin-layer chromatographic screening and optimization. Six plates could be developed simultaneously with six different solvent systems. Bed lengths could be varied continuously up to 8 cm. With this system, the plates could be placed in the chamber at the end of the day; results were available the next morning. The use of individual reservoirs resulted in very little solvent being used.

For optimization of the dichlorobenzophenone continuous TLC system, several solvent systems were prepared by diluting the optimized conventional TLC system, carbon tetrachloride/benzene (4:1), with cyclopentane. The ratio of conventional solvent systems to cyclopentane was varied in the following proportions -- 0:100, 1:100, 2:100, 5:100, and 10:100. Development of the plates was terminated when the more mobile sample zone approached 0.5 cm from the solvent evaporation line. The bed lengths investigated in this work were 4, 5, 6, and 8 cm. The 8-cm plate was allowed to run overnight. Zones were visualized by exposure to short-wavelength ultraviolet light (approximately 254 nm) after a 30-min exposure of the plate to iodine vapors.

In the reversed-phase mode, the TLC plates ($KC_{18}F$, 20 cm x 20 cm, Whatman Chemical Separation, Inc., Clifton, New Jersey 07014) were developed over a 15-cm bed in a conventional TLC chamber. The developing solvents investigated consisted of methanol and water mixtures. The proportion of water was varied from 0 to 25%. The concentrations of benzophenones and the amount applied to the plate were the same as those described above for the continuous development. The separated zones were detected by irradiation with short-wavelength ultraviolet light.

RESULTS AND DISCUSSION

Advantages and characteristics of continuous development over a short chromatographic bed have been discussed in detail by Perry (13). The results obtained with the benzophenone isomers tend to support his general conclusion that this approach to TLC may be used to advantage for select difficult TLC separations. Improved separation of the benzophenone isomers over conventional development on silica gel plates was achieved using the continuous development system. With the utilization of a more nonpolar developing solvent and a short bed length, it was possible to determine 1% of the 2,3'- isomer and 5% of the 2,2'- isomer in the presence of 2,4'-dichlorobenzophenone. This separation was obtained using a ratio of cyclopentane to conventional solvent, carbon tetrachloride/benzene (4:1), of 100:10 and an 8-cm bed length. The mobility of 2,4'-dichlorobenzophenone was intermediate between the two isomers, the 2,3'- isomer being the more mobile. For an overnight development (approximately 16 hrs), the relative mobility of the 2,4'-, 2,3'-, and 2,2'- isomers was 1.00, 1.19, and 0.81, respectively. The 8.0-cm bed was necessary to resolve the 2,2'- and 2,3'- compounds from the large amount of the 2,4'- isomer (28 μg) applied to the plate.

Reversed-phase TLC was found to be complementary to the continuous development TLC for the separation of dichlorobenzophenone isomers. Several reversed-phase systems were investigated. While the 2,3'- and 2,4'- dichlorobenzophenones could not be resolved, complete separation of 2,4'-dichlorobenzophenone and the 2,2'- isomer was obtained using a developing solvent of methanol and water (60:10). The R_f values for the 2,2'-, 2,3'-, and 2,4'- isomers with this solvent system were 0.55, 0.45, and 0.45, respectively. Using this solvent system, we were able to detect 1% of the 2,2'- isomer in the synthetic intermediate of interest; namely, the 2,4'- isomer. The development time was about 60 min.

In summary, a preliminary purity evaluation of 2,4'-dichlorobenzophenone can be made using the two simple TLC procedures reported in this work. The methods are complementary, and both are quite applicable to a production situation. In combination, they can be used to determine whether the synthetic 2,4'-dichlorobenzophenone meets existing specifications of allowable isomeric impurities.

ACKNOWLEDGMENT

The authors wish to thank Dr. T. J. Kress (Lilly Research Laboratories) for supplying authentic samples of the isomeric dichlorobenzophenones used in this work.

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