TLC Mesh Column Chromatography: Facile Combination of Vacuum-Driven and Low-Pressure Methods

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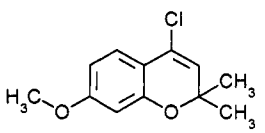
Due to the constant need in synthetic organic chemistry to separate mixtures of small or large quantities with the best possible result, common column chromatographic methods have been significantly improved in the last two decades. A column chromatographic method can be characterized from a practical point of view with the following requirements: resolution, time needed for the separation, cost of the system, and convenience.

TLC mesh column chromatography[1] (vacuum or low-pressure driven) has very good resolution and the time needed for the separation is not long. The system is inexpensive, but in the case of vacuum-driven method manipulation of the eluate is rather difficult and the maximum pressure differential (1 bar) between the top and the bottom of the column limits the variability of the flow rates. In the case of the low-pressure method the packing and compacting of the bed and the application of the sample are inconvenient and in some cases the expulsion of air is not sufficient.[2]

We outline here a combined TLC mesh column chromatographic system that unifies the advantages of the vacuum-driven and low-pressure methods and can be considered as an improvement of Taber's method.[1] The first part of the chromatography, from packing until the solvent front has reached the bottom of the bed, is conducted under vacuum. Here we utilize the advantage of the vacuum-driven method where any manipulation at the top of the column can be achieved at will because it is at atmospheric pressure. Then the vacuum is broken and pressure is applied to the top of the column. In that part of the separation eluate manipulation can be easily done because the bottom of the bed is at atmospheric pressure. These modifications make our method efficient and convenient to use.

Our procedure was found to be efficient for separations of mixtures showing $\Delta R_f \geq 0.05$ by TLC. In comparison with Taber's low-pressure method[1] we achieved the same or better separations.[3]

To test the system on a preparative scale, 1 g of a 1:1 mixture of 4-chloro-7-methoxy-2,2-dimethyl-2*H*-chromene[4] (**1**) and 3,4-dichloro-7-methoxy-2,2-dimethyl-2*H*-chromene[5] (**2**) ($\Delta R_f = 0.06$ by TLC) was quantitatively separated on 50 g of silica gel[6a] using 1,2-dichloroethane–hexane (1:8) as eluent. Column diameter = 35 mm, height/diameter = 4.6, fraction volume = 25 mL, number of fractions = 29. **2** appeared in fractions nos. 9–14 (495 mg) and **1** in fractions nos. 17–23 (491 mg). In fraction nos. 15–16 no material was detected by TLC. Time of the separation = 45 min.



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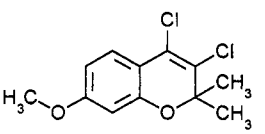

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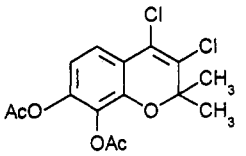
Table 1. Typical Parameters Where Height/Diameter Ratio = 6 and the Mass of the Gel/Mass of the Sample = 50

no.	column internal diameter (mm)	mass of silica gel (g)	height of the bed (mm)	sample size (g)	fraction volume (mL) manual collecting	fraction volume (mL) automatic collecting
1	15	5.1	90	0.10	5	5
2	25	23.6	150	0.47	20	20
3	35	64.6	210	1.30	50	25
4	45	135	270	2.70	120	25

To compare our method with Taber's low-pressure method,[1] 1.3 g of a 1:1 mixture of 7,8-diacetoxy-3,4-dichloro-2,2-dimethyl-2*H*-chromene[7] (**3**) 7,8-diacetoxy-4-chloro-2,2-dimethyl-2*H*-chromene[7] (**4**) ($\Delta R_f = 0.05$ by TLC) was separated by both methods using 1,2-dichloroethane–hexane (1:3) as eluent and silica gel.[6a] For



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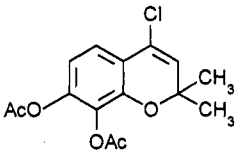

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parameters see Table 1, no. 3. In both cases quantitative separation was achieved. In the course of our work we improved Taber's low-pressure method, making it more practical and convenient to use and possessing the same resolution and recovery factor.

Experimental Section

First Part: Column packing. Single portion, vacuum dry-pack method is used.[3] The sorbent[6a,b] is poured into the column and allowed to settle by gravity. Manual tapping helps to eliminate the major air pockets. Vacuum was applied (Figure 1) to the column by opening the stopcock (C) to compact the sorbent. Its total compression was approximately 30% by volume. Then the stopcock (C) is closed.

Sample Application. The solution of the mixture to be separated is slurried with coarse silica gel[1,8] and the solvent removed under vacuum. This dry gel is applied to the top of the column to make an even layer. Subsequently the top is covered with a layer of sand to at least 1-in. depth.

Elution. The first part of the elution is performed under vacuum[3,9] that is applied to the system until the eluent front has passed through the length of the bed and a few milliliters of eluent has been collected. Then the stopcock (C) is closed and the vacuum is released. The collecting vessel is removed (D).

Second Part: The fraction collector (J) is connected to the end of the column and a screw-thread connector is secured to the

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(2) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(3) Targett, N. M.; Kilcoyne, J. P.; Green, B. *J. Org. Chem.* **1979**, *44*, 4962.
(4) Eszenyi, T.; Tímár, T.; Sebök, P. *Tetrahedron Lett.* **1991**, *32*, 827.
(5) Camps, F.; Coll, J.; Messeguer, A.; Pericás, M. A. *Tetrahedron Lett.* **1979**, *20*, 3901.
(6) (a) MN-Kieselgel N-HR purchased from Macherey Nagel Co. (Germany). (b) TLC Silica gel 60H (mean particle size 15 μm), purchased from E. Merck, was used.
(7) Zsótér, Zs.; Eszenyi, T.; Tímár, T. *Tetrahedron Lett.*, submitted.
(8) Silica gel 60 (63–200 μm) was purchased from E. Merck.
(9) We use the central vacuum system in our laboratory (20–80 mmHg).

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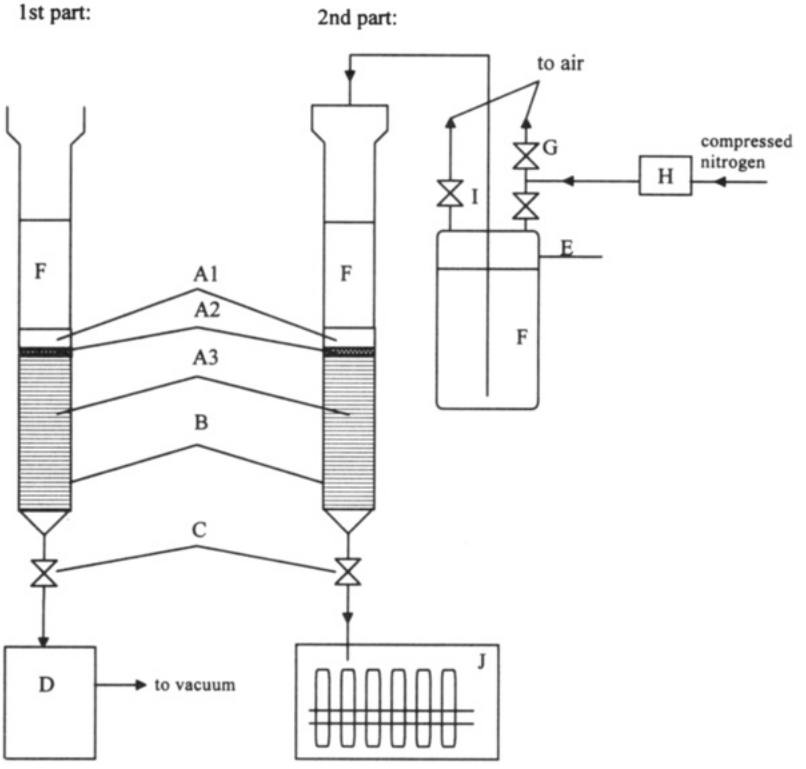

Figure 1. The apparatus and some specifications: A_1, sand layer; A_2, preadsorbent layer; A_3, sorbent; B, column; C, column isolation stopcock; D, collecting vessel; E, eluent reservoir; F, eluent; G, relief valve; H, three-stage regulator; I, relief stopcock; J, automatic fraction collector.

top. The connection between the connector and the eluent reservoir is a flexible metal tube. The reservoir[10] (E) is then pressurized[11,12] and the stopcock (C) is opened; the elution is continued. The change over takes no more than 1–2 min.

(10) The reservoir should be equipped with a relief stopcock. A relief valve is also recommended.

Acknowledgment. We thank Gábor Répási and Sándor Garadnay for their technical help.

(11) We use compressed nitrogen reduced by a three-stage regulator to 1–2.5 bar.

(12) Although we have run many separations without any difficulty, glass columns coated with transparent adhesive tape are recommended for safety reasons.