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Note

Convenient apparatus for methylating small samples with diazomethane

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Schlenk and Gellerman¹ introduced a method for small-scale esterification of fatty acids with diazomethane in 1960. Methylation by that procedure is now commonly used to increase the volatility and improve the chromatographic characteristics of a wide range of acidic organic compounds. However the explosive and toxic nature of diazomethane² mandates a sealed but flexible system that minimizes leakage and glassware breakage yet provides for convenient attachment and removal of sample and reaction vials to the methylation system. Contaminants from non-inert surfaces, such as rubber stoppers, should also be eliminated in order to achieve accurate quantitative results with modern, high-performance, chromatographic columns. Experience in our laboratory has shown that previously described apparatus^{1,3} used in the production of diazomethane lack one or more of these requirements. As a result we have modified the Schlenk and Gellerman system and have developed a simple, inert and tightly-sealed unit that allows for convenient methylation of small samples.

The completely assembled apparatus consists of four identical units (Fig. 1) connected in series with PTFE tubing. A stream of nitrogen is passed through 8 ml of diethyl ether in the first unit and then into the diazomethane generating unit (unit 2) that contains 1.1 ml of diethyl ether, 1.1 ml (2-(2-ethoxyethoxy) ethanol (Aldrich, Milwaukee, WI, U.S.A.), 0.9 ml of 10 M NaOH and 0.8 g of N-methyl-N-nitroso-*p*-toluene sulfonamide (Diazald, Aldrich). Ethereal diazomethane is swept into unit three which, initially, contains 3 ml of diethyl ether. When the ether turns yellow, the vial is replaced with one containing a sample dissolved in 3 to 6 ml of methanol or another appropriate solvent. Derivatization is complete upon development of a light yellow color in the sample vial. Excess diazomethane passes into unit 4 and is neutralized in 8 ml of glacial acetic acid. Six to eight samples of μg to mg quantities can be esterified in about 10 min. The reaction in unit 2 is stopped by adding 3 ml of acetic acid, and the reagents are replaced before repeating the procedure with additional samples.

Each unit consists of a 6 mm O.D. gas delivery tube (g) with the inlet tapered to allow attachment of narrow-bore PTFE tubing. All cut glass is fire polished to avoid reactive surfaces². The delivery tube is held in place with a bored vial cap (a), and a closed, leak-proof system is assured by using PTFE-backed, silicone, sealing rings (b, 15 mm O.D., 6 mm I.D. and d, 22 mm). The flanged, double screw-cap (e, 22 mm) facilitates rapid changing of sample vials (f). Excess diazomethane leaves the unit via

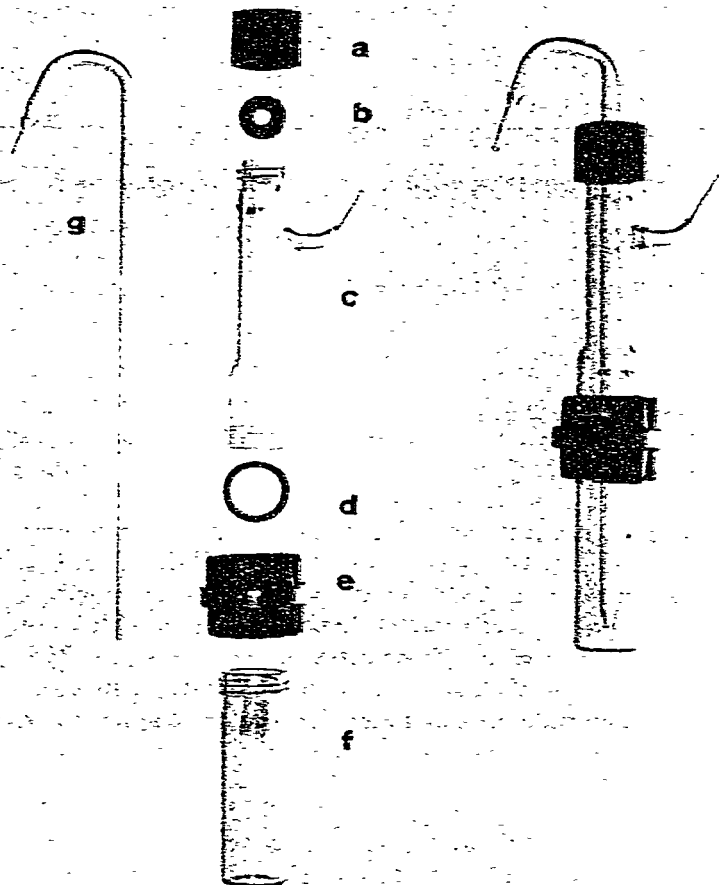


Fig. 1. An assembled methylation unit and individual components. Description in text.

the tapered outlet of part c which consists of two fused, glass screw joints (22 and 15 mm). All parts of the apparatus are available from Sovirel Laboratory Glassware (Levallois-Perret, France) or from Pegasus Industrial Specialties (Agincourt, Ontario, Canada) and modifications are simple and readily made by a competent glassblower.

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