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Note

Thin-layer chromatographic procedure for the differentiation of the optical isomers of cocaine

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Medicinally used cocaine is prepared from the leaves of the coca plant (*Erythroxylon coca*, Lamarck) by extracting the total alkaloids and converting them to *l*-ecgonine by acid hydrolysis. The isolated *l*-ecgonine is esterified with methanol and benzoic acid to produce the natural product, *l*-cocaine[1]. In 1923 a method for the synthesis of *dl*-cocaine was published[2]. The racemic mixture was separated into the *dextro* and *levo* isomers of cocaine with tartaric acid[2]. Probably all of the currently available illicit cocaine is prepared from coca leaves and therefore is the natural isomer *l*-cocaine. However, there is the possibility of the occurrence of synthetic *dl*- or *d*-cocaine in illegal drugs and, for legal reasons, it may be necessary for the forensic chemist to be able to distinguish between the optical isomers. The following method was developed for this purpose and makes possible the routine analysis of small samples of illicit cocaine and the determination of the optical isomer or isomers present in the sample. Cocaine was hydrolysed to ecgonine and then esterified with the enantiomeric 2-octanols to give the necessary derivatives. The resulting diastereoisomers may be distinguished by thin-layer chromatography (TLC).

EXPERIMENTAL

Materials and methods

The *dl*-cocaine was prepared by benzoylation of *dl*-methylecgonine[2] and the *d*-cocaine by resolution of *dl*-cocaine[2]. The *l*-cocaine and the benzenesulfonyl chloride were obtained commercially (E. Merck, Darmstadt, G.F.R.) as well as the *d*-2-octanol, *l*-2-octanol and *dl*-2-octanol (Fluka, Buchs, Switzerland).

The diastereomeric derivatives were prepared in 0.3 ml Reacti-Vials® provided with magnetic stirrers (Pierce Chem. Co., Rockford, Ill., U.S.A.) according to the procedure of Brewster and Ciotti[3].

TLC separation of the isomers was carried out on non-activated pre-coated silica gel plates of thickness 0.25 mm (E. Merck) with methanol as the developing solvent.

Procedure

Approximately 0.5 mg of cocaine base or hydrochloride was placed in a 0.3 ml

screw-cap vial and 30 μl of 2 *N* hydrochloric acid were added. The vial was capped and heated for 30 min in a heating block maintained at 120°. The cap was removed and the heating continued for about 20 min to evaporate the solvent completely. The residue was allowed to cool to room temperature, then 30 μl of pyridine were added, followed by 3 μl of *d*-2-octanol and the vial was placed in a small dish with water and ice. After cooling for some minutes 1 μl of benzenesulfonyl chloride was added. The vial, provided with a magnetic stirrer, was capped and stirred slowly (60 rpm) for 30 min while the solution was kept cold. Then 30 μl of 2 *N* ammonia were added, followed by 100 μl of ether and the mixture was stirred rapidly for a short time.

Then 2 μl of the ether layer were placed on the starting line of the TLC plate. The plates were developed in cylindrical glass vessels (without prior equilibration) with methanol until the solvent front had reached a height of 15 cm. The plates were air dried at room temperature and sprayed with acidified iodoplatinate[4]. The two reference spots were obtained by using the same procedure with *l*-cocaine and *d*-2-octanol and with *l*-cocaine and *l*-2-octanol or, more simply, with *l*-cocaine and *dl*-2-octanol.

RESULTS AND DISCUSSION

The method for the preparation of esters with benzenesulfonyl chloride in pyridine[3] was found to be the most convenient, giving a high yield in a short time. The optically active alcohols, menthol, borneol, 2-methyl-1-butanol and 2-octanol, were used to prepare esters of *dl*-ecgonine in this way. The TLC separation was best when the diastereoisomers prepared from 2-octanol were used. The R_F values of the diastereoisomers of 2-octanyl-ecgonine are shown in Table I. After spraying with acidified iodoplatinate[4] the spots were intense blue-green, discrete and well defined. In case of double spots of equal amounts of the diastereoisomers, the spot with the high R_F value was always distinctly smaller than the other spot.

TABLE I

SEPARATION OF DIASTEREOISOMERS OF 2-OCTANYLECGONINE BY THIN-LAYER CHROMATOGRAPHY

Ester prepared from	R_F
l-Ecgonine and *d*-2-octanol	0.36
l-Ecgonine and *l*-2-octanol	0.28
l-Ecgonine and *dl*-2-octanol	0.28, 0.36
d-Ecgonine and *d*-2-octanol	0.28
d-Ecgonine and *l*-2-octanol	0.36
d-Ecgonine and *dl*-2-octanol	0.28, 0.36
dl-Ecgonine and *d*-2-octanol	0.28, 0.36
dl-Ecgonine and *l*-2-octanol	0.28, 0.36

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