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Note

Thin-layer and short-column chromatography of epimeric alcohols of some quinolizidine derivatives

W. WYSOCKA

Department of Organic Chemistry, University of Poznań, Poznań–Grunwaldzka 6 (Poland)

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During our study of the stereochemical course of the reduction of some quinolizidin-2-one derivatives, it was found that the oxo group of 13-oxolupanine (I) could be stereoselectively transformed, depending on the medium used in catalytic hydrogenation [in the presence of platinum (IV) oxide], into either an equatorial or an axial hydroxy group[1]. Alternatively, the oxo group can be reduced in one stage to a methylene-group[1]. It was also found that, depending on the molar ratio of hydrochloric acid to I, catalytic hydrogenation results in a mixture of epimeric alcohols or, in another experiment, in a mixture of epimeric alcohols and the hydrogenolysis product[2]. The latter achievement was possible owing to an elaborate and efficient method of separation by chromatography. The use of thin-layer chromatography (TLC) permitted formation of the epimeric alcohols to be controlled, and their separation was achieved on a preparative scale by "short-column" chromatography[3].

In this paper, we report the application of TLC and "short-column" chromatography for the separation of two pairs of epimeric alcohols of the same quinolizidine derivatives, *viz.*, 13-hydroxylupanine (II) and *epi*-13-hydroxylupanine (III), and 13-hydroxy-α-isolupanine (IV) and *epi*-13-hydroxy-α-isolupanine (V).

EXPERIMENTAL

TLC was carried out on glass plates (5 × 20 cm) coated with a 0.25-mm thick layer of silica gel HF_{254} (Merck, Darmstadt, G.F.R.). The plates were air dried. After development, the compounds were located with iodine vapour. Several developing systems were used, of which three are considered here:

(A) Chloroform–ethanol (3:2)
(B) Benzene–methanol (4:1)
(C) Ethyl acetate–chloroform–benzene (2:2:1).

RESULTS AND DISCUSSION

II and III differ from IV and V only in the configuration of the C–D fragment of the molecule; II and III consist of two quinolizidine systems with *trans–cis* ring-fusion, whereas IV and V have two *trans*-quinolizidine systems.

The three solvent systems A, B and C were used with success to resolve the two pairs of epimeric alcohols. The equatorial epimers always had R_F values higher

than those of the axial epimers. The epimeric alcohols from the *trans–trans* ring-fused quinolizidine were the most rapidly moving compounds in all of the solvent systems tested. The best resolution of both pairs of epimeric alcohols was achieved in system A.

PREPARATIVE-SCALE RESOLUTION OF EPIMERS II AND III

For this purpose, "short-column" chromatography was used[3], with a column of silica gel HF_{254} and system A as mobile phase. The separation was achieved on a 25 × 2 cm column; a cylindrical vessel with a sintered disc was used as column support, and the column was topped by a head connected with an aquarium-aeration pump.

A Whatman 41 filter-paper was laid over the sintered disc, and 7 g of the silica gel was shaken briskly for 1 min in a stoppered flask with 15 ml of solvent A; the moderately thin slurry was then carefully transferred to the column with a large pipette, which reached well down into the vessel. The column was left vertical and undisturbed until the gel had bedded down, which took about 1 h; it was ready for use by the time the surface of the descending liquid had reached the top of the gel. The height of the gel layer after bedding down was 4 cm.

An open-texture filter-paper (Whatman 41) was then placed over the surface, and the supernatant solvent was allowed to drain into the gel, then an even layer (1.5 mm thick) of washed sand was added to facilitate uniform distribution of the material to be chromatographed. This material (100 mg of the mixture of alcohols II and III) was dissolved in 1 ml of chloroform, and the solution was added centrally, by pipette, to the surface of the sand. The column was then very carefully filled up with solvent, and the pump was started. Twenty-five fractions, each of about 3 ml, were collected, and the flow-rate was 0.8 ml/min. The separation was quantitative, 75 mg of III and 25 mg of II being obtained.

Separation of the epimers by "short-column" chromatography was much more efficient than that achieved on conventional columns, and was attained in only one twentieth of the time needed with a conventional column. Also, the volume of solvent required was only 2% of that necessary with a larger column. This method has also been successfully applied to the resolution of other epimeric alcohols. Results for compounds II, III, IV and V are shown in Table I

TABLE I

SEPARATION OF EPIMERIC ALCOHOLS OF SOME QUINOLIZIDINE DERIVATIVES

For compositions of the mobile phases A, B and C see text.

Compound	R_F		
	A	*B*	*C*
II	0.92	0.93	0.87
III	0.76	0.82	0.83
IV	0.83	0.83	0.79
V	0.54	0.75	0.66

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