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Note

Steroids and related studies

LVI. Thin-layer chromatography of some azasteroids

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Previously we have carried out thin-layer chromatographic (TLC) studies with some steroidal ketones[1,2], oximes[1,2], amides[2], lactams[1–3], tetrazoles[2,3] and basic and quaternary azasteroids[3]. In this paper we report the results of chromatographic studies on different azasteroids, which include secondary and tertiary bases, hydrochloride salts of certain tertiary bases and mono- and bisquaternary iodides.

EXPERIMENTAL

Azasteroids

Several of the basic and quaternary azasteroids were prepared in our laboratory. Appropriate references to the reported methods of preparation are given in the tables.

Adsorbent and TLC plates

Silica gel G (E. Merck, Darmstadt, G.F.R.) was mixed with distilled water (30 g in 60 ml of water) and coated on 20 × 20 cm plates to a thickness of 0.25 mm. The plates were air-dried for 15 min, heated at 110°C for 1 h and then stored in a cabinet over calcium chloride.

The running distance was 16 cm at a temperature of 25–30°C, and the amount of an azasteroid applied was 50–100 μg.

Detection

Cerium(IV) sulphate solution (2 g in 100 ml of 10% sulphuric acid) was used as the spray reagent, followed by heating at 150°C for 30 min, which gave permanent black spots. Exposure to iodine vapour was also used and gave brown spots in 2–4 min.

Solvents

All of the solvents employed were of analytical reagent grade and were used without further treatment; the strong ammonia solution used was 30% (w/w). The following solvent systems were tried:

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(1) methanol–strong ammonia solution (9:1)
(2) ethanol–strong ammonia solution (9:1)
(3) ethyl acetate–1-propanol–strong ammonia solution (40:30:3)
(4) 1-butanol–ethanol–strong ammonia solution (6:3:1)
(5) ethanol–chloroform–ethyl acetate–water (4:2:2:1)
(6) methanol–strong ammonia solution (1:1)
(7) 1-butanol–acetic acid–water (5:4:3)
(8) ethanol–ethyl acetate–chloroform–water–concentrated hydrochloric acid (120:48:32:20:1)
(9) ethanol–concentrated hydrochloric acid–chloroform–ethyl acetate–water (20:12:10:10:5)

TABLE I

THIN-LAYER CHROMATOGRAPHY OF SOME BASIC AZASTEROIDS IN SOLVENT SYSTEMS 1–4

Compound	R_F *value*			
	1	*2*	*3*	*4*
4-(2-Hydroxyethyl)-4-aza-5α-cholestane[4]	0.76	0.72	0.75	0.74
3-Pyrrolidino-17a-aza-D-homo-5α-androst-2-en-17-one[5]	0.77	0.69	0.54	0.67
3β-Pyrrolidino-17a-aza-D-homo-5α-androstan-17-one[5]	0.61	0.64	0.44	0.64
3β-Pyrrolidino-17a-aza-D-homo-5α-androstane[5]	0.22	0.28	0.10	0.37
17a-Ethyl-3-pyrrolidino-17a-aza-D-homoandrosta-3,5-diene[5]	0.63	0.65	0.44	0.58
17a-Ethyl-3β-pyrrolidino-17a-aza-D-homoandrost-5-ene[5]	0.55	0.63	0.39	0.65
17a-Methyl-3β-pyrrolidino-17a-aza-D-homo-5α-androstane[5]	0.43	0.53	0.19	0.57
17a-(2-Hydroxyethyl)-3-pyrrolidino-17a-aza-D-homoandrosta-3,5-diene[4]	0.65	0.69	0.42	0.57
17a-(2-Hydroxyethyl)-3β-pyrrolidino-17a-aza-D-homoandrost-5-ene[4]	0.50	0.60	0.41	0.66
4,17a-Diethyl-4,17a-diaza-D-homo-5α-androstane[6]	0.46	0.58	0.45	0.66
4-(2-Hydroxyethyl)-4-aza-5α-androstan-17β-ol[4]	0.76	0.72	0.69	0.70
4,17a-Di(2-hydroxyethyl)-4,17a-diaza-D-homo-5α-androstane[7]	0.61	0.65	0.38	0.60
4-(2-Chloroethyl)-4-aza-5α-androstan-17β-ol[7]	0.57	0.63	–	0.60
17a-Aza-D-homoandrost-4-en-3-one[8]	0.31	0.30	0.12	0.34
17a-Ethyl-17a-aza-D-homoandrost-5-en-3β-ol[5]	0.61	0.65	0.54	0.69
17a-Ethyl-17a-aza-D-homoandrost-4-en-3-one[5]	0.59	0.70	0.52	0.64
17a-(2-Hydroxyethyl)-17a-aza-D-homoandrost-5-en-3β-ol[4]	0.69	0.69	0.56	0.65
17a-(2-Hydroxyethyl)-17a-aza-D-homoandrost-4-en-3-one[4]	0.70	0.68	0.52	0.64
17a-(2-Acetoxyethyl)-17a-aza-D-homoandrost-5-en-3β-yl acetate[4]	0.71	0.69	0.62	0.67

TABLE II

THIN-LAYER CHROMATOGRAPHY OF HYDROCHLORIDES OF CERTAIN TERTIARY AZASTEROIDS IN SOLVENT SYSTEMS 5, 7–9

Compound	R_F *value*			
	5	*7*	*8*	*9*
4-(2-Acetoxyethyl)-4-aza-5α-cholestane hydrochloride[4]	0.65	0.61	0.75	–
4-(2-Chloroethyl)-4-aza-5α-cholestane hydrochloride[7]	0.69	0.66	0.70	–
4-(2-Chloroethyl)-4-aza-5α-androstan-17β-ol hydrochloride[7]	–	–	–	0.67
3β-Chloro-17a-(2-chloroethyl)-17a-aza-D-homoandrost-5-ene hydrochloride[7]	0.53	0.58	0.68	–

TABLE III

THIN-LAYER CHROMATOGRAPHY OF SOME MONO- AND BISQUATERNARY AZASTEROIDS IN SOLVENT SYSTEMS 5–9

Compound	R_F *value*				
	5	*6*	*7*	*8*	*9*
4-(2-Hydroxyethyl)-4-aza-5α-cholestane methiodide[4]	0.48	–	0.63	0.65	–
4-(2-Acetoxyethyl)-4-aza-5α-cholestane methiodide[4]	0.67	–	0.60	0.68	–
4-(2-Hydroxyethyl)-4-aza-5α-androstan-17β-ol methiodide[4]	–	0.59	–	0.61	–
4-(2-Acetoxyethyl)-4-aza-5α-androstan-17-β-yl acetate methiodide[4]	–	0.61	0.46	0.47	–
17a-(2-Hydroxyethyl)-17a-aza-D-homoandrost-5-en-3β-ol methiodide[4]	–	0.58	0.40	0.42	–
17a-(2-Acetoxyethyl)-17a-aza-D-homoandrost-5-en-3β-yl acetate methiodide[4]	0.21	0.58	0.42	0.52	–
17a-Ethyl-3β-pyrrolidino-17a-aza-D-homoandrost-5-ene diethiodide[5]	–	–	–	–	0.47
17a-(2-Hydroxyethyl)-3β-pyrrolidino-17a-aza-D-homoandrost-5-ene dimethiodide[4]	–	–	–	–	0.39
17a-(2-Acetoxyethyl)-3β-pyrrolidino-17a-aza-D-homoandrost-5-ene dimethiodide[4]	–	–	–	–	0.39
17a-Methyl-3β-pyrrolidino-17a-aza-D-homoandrost-5-ene diethoiodide[5]	–	–	–	–	0.47
17a-Methyl-3β-pyrrolidino-17a-aza-D-homo-5α-androstane diethiodide[5]	–	–	–	–	0.31
17a-Methyl-3β-pyrrolidino-17a-aza-D-homo-5α-androstane dimethiodide[5]	–	–	–	–	0.32

RESULTS

In Table I are listed the R_F values of basic azasteroids, which were secondary and tertiary amines. Solvent systems 1–4 gave consistent results; systems 2 and 4 are best since the R_F values are relatively higher.

The R_F values of the hydrochlorides of some tertiary azasteroids are given in Table II. Of the solvent systems useful for the hydrochloride salts (5, 7–9), system 8 was best, except for one salt which was more mobile in system 9.

Table III lists the R_F values of some mono- and bisquaternary azasteroids in solvent systems 5–9. For monoquaternary iodides, systems 7 and 8 were suitable and 9 worked well with bisquaternary iodides.

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