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Note

Steroids and related studies

L.* Thin-layer chromatography of some steroidal ketones, oximes, amides, lactams and tetrazoles

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For a number of years, we have been working on different aspects of azasteroids. Previously, we have described thin-layer chromatographic (TLC) studies[1,2] with different steroidal ketones, oximes, lactams, tetrazoles and quaternary azasteroids. Here, we provide TLC data on several other ketones, oximes, amides, lactams and tetrazoles.

EXPERIMENTAL

Steroid derivatives

Most of the steroids used as starting materials and ketones (Table I), oximes (Table II), amides and lactams (Table III) and tetrazoles (Table IV and V) were prepared in our laboratory. References to the methods of preparation of the compounds 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 per 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° for 60 min, then stored in a drying cabinet over calcium chloride.

The running distance was 16 cm at a temperature of 23–26°, and the load of steroid derivative 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° for 30 min, which gave permanent black spots. Exposure to iodine vapour was also used and gave brown spots in 2–4 min.

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* For Part IL, see H. Singh, K. K. Bhutani, R. K. Malhotra and D. Paul, *J. Chem. Soc., Perkin Trans. I*, in press.

TABLE I

R_F VALUES OF STEROIDAL KETONES AND CERTAIN OTHER STARTING MATERIALS IN SOLVENT SYSTEMS 1–6

Compound	*Solvent system*					
	1	*2*	*3*	*4*	*5*	*6*
Pregn-5-ene-3β,20β-diol diacetate[3]	0.68	0.59	0.63	0.81	—	—
Pregn-5-ene-3β,20β-diol[4]	—	—	0.11	0.12	0.38	0.23
Androst-5-ene-3β,17β-diol diacetate[5]	0.62	0.56	0.61	0.78	—	—
Androst-5-ene-3β,17β-diol[5,6]	—	—	0.08	0.10	0.33	0.19
Androst-4-en-3-one[7]	0.54	0.42	0.53	0.57	—	—
7-Oxopregn-5-ene-3β,20β-diol diacetate[4]	—	0.30	0.29	0.52	0.87	—
7-Oxoandrost-5-ene-3β,17β-diol diacetate[8]	0.33	0.23	0.26	0.35	—	—
3β-Hydroxycholest-5-en-7-one[9]	—	—	0.08	0.08	0.41	0.19
Cholesta-3,5-dien-7-one[10]	0.76	0.70	0.71	0.84	—	—
Cholest-5-ene-3,7-dione[9]	0.33	—	0.54	0.51	—	0.44
Pregna-3,5-diene-7,20-dione[11]	—	0.36	0.34	0.52	0.88	—
(25*R*)-12-Oxo-5α-spirostan-3β-yl acetate[12] (hecogenin acetate)	0.49	0.40	0.51	0.48	—	—
5-Oxo-3,5-seco-4-norcholestan-3-oic acid[13]	—	—	0.07	0.04	0.17	0.15

TABLE II

R_F VALUES OF STEROIDAL KETOXIMES IN SOLVENT SYSTEMS 5, 7, 8 AND 9

Compound	*Solvent system*			
	5	*7*	*8*	*9*
(25*R*)-3-Hydroxyiminospirost-4-ene[14]	0.52	0.54	0.41	0.34
		0.47	0.33	
6-Hydroxyimino-5α-cholestan-3β-yl acetate[9]	0.76	0.66	0.52	0.57
(25*R*)-12-Hydroxyimino-5α-spirostan-3β-yl acetate[15]	0.79	0.74	0.52	0.64
17-Hydroxyiminoandrost-5-en-3β-yl acetate[16]	0.58	0.48	0.32	0.39
17-Hydroxyimino-5α-androstan-3β-yl acetate[17]	0.60	0.50	0.34	0.41
17-Hydroxyimino-5α-androstan-3β-ol[17]	0.22	0.18	0.09	0.16
20-Hydroxyiminopregn-5-en-3β-yl acetate[18]	0.73	0.66	0.55	0.52
20-Hydroxyiminopregna-5,16-dien-3β-yl acetate[16]	0.83	0.72	0.63	0.68
	0.42	0.51	0.44	0.45
3,17-Dihydroxyiminoandrost-4-ene[16]	0.18	0.27	0.13	0.12
	0.10	0.12	0.05	0.07
5-Hydroxyimino-3,5-seco-4-norcholestan-3-oic acid[13]	0.09	0.09	0.05	0.05

TABLE III

R_F VALUES OF STEROIDAL AMIDES AND LACTAMS IN SOLVENT SYSTEMS 10–15.

Compound	*Solvent system*					
	10	*11*	*12*	*13*	*14*	*15*
17β-Acetamidoandrost-5-en-3β-yl acetate[19]	0.56	0.57	0.50	0.50	0.67	0.57
17β-Acetamidoandrost-4-en-3-one[20]	—	0.46	0.49	0.41	0.52	0.47
17β-Acetamido-7-oxoandrost-5-en-3β-yl acetate[21]	0.44	0.50	0.46	0.42	0.54	0.46
4,20-Dioxo-3-aza-4-homopregn-4a-eno[17α,16α-*c*]-1′-pyrazoline[22]	0.34	0.35	0.52	0.44	0.40	0.35
(25*R*)-12-Oxo-12a-aza-C-homo-5α-spirostan-3β-yl acetate[15]	0.72	0.67	0.66	0.67	0.77	0.68
12,20-Dioxo-12a-aza-C-homo-5α-pregn-16-en-3β-yl acetate[15]	0.56	0.51	0.50	0.46	0.53	0.53
17-Oxo-17a-aza-D-homo-5α-androstan-3β-yl acetate[17]	0.47	0.43	0.50	0.45	0.58	0.42
3β-Hydroxy-17a-aza-D-homo-5α-androstan-17-one[17]	0.24	0.31	0.44	0.31	0.38	0.22
17a-Aza-D-homo-5α-androstane-3,17-dione[23]	0.52	0.35	0.50	0.39	0.41	0.41
3,7a-Diaza-A,B-bishomocholest-5-ene-4,7-dione[24]	0.17	0.21	0.46	0.19	0.35	0.33

Solvents

All of the solvents employed were of analytical-reagent grade and were used without further treatment. The following solvent systems were tried: (1) chloroform–methanol (397:3); (2) benzene–ethyl acetate (7:1); (3) *n*-hexane–ethyl acetate (3:1); (4) chloroform–ethanol (99:1); (5) chloroform–methanol (39:1); (6) benzene–ethyl acetate (7:3); (7) benzene–ethyl acetate (13:7); (8) *n*-hexane–ethyl acetate (7:3); (9) chloroform–ethanol (97:3); (10) chloroform–methanol (19:1); (11) ethyl acetate–chloroform–methanol (13:5:2); (12) benzene–methanol (4:1); (13) benzene–methanol–ethyl acetate (15:3:2); (14) *n*-hexane–ethyl acetate–methanol (10:7:3); (15) methylene

TABLE IV

R_F VALUES OF STEROIDAL TETRAZOLES IN SOLVENT SYSTEMS 10, 11, 12, 13, 15, 16 AND 17

Compound	*Solvent system*						
	10	*11*	*12*	*13*	*15*	*16*	*17*
16β-Bromo-17α-hydroxy-3-aza-A-homopregn-4a-eno[3,4-*d*]tetrazol-20-one[25]	—	0.68	0.65	0.65	0.71	0.60	0.58
16β-Chloro-17α-hydroxy-3-aza-A-homopregn-4a-eno[3,4-*d*]tetrazol-20-one[25]	—	0.69	0.64	0.67	0.71	0.59	0.57
17α-Hydroxy-16β-thiocyanato-3-aza-A-homopregn-4a-eno[3,4-*d*]tetrazol-20-one[25]	—	0.70	0.61	0.62	0.66	0.55	0.52
6-Aza-B-homo-5α-cholestano[6,7-*d*]tetrazol-3β-ol[26]	—	0.60	0.59	0.58	0.49	0.45	0.55
4,7a-Diaza-A,B-bishomocholest-4a-eno[7a,7-*d*]-tetrazol-3-one[27]	—	0.44	0.53	0.44	0.33	0.39	0.38
20-Oxo-7a-aza-B-homopregna-5,16-dieno[7a,7-*d*]-tetrazol-3β-yl acetate[28,29]	—	0.71	0.73	0.72	0.83	0.80	0.70
20-Oxo-7a-aza-B-homopregn-5-eno[7a,7-*d*]tetrazol-3β-yl acetate[21,28,29]	—	0.72	0.69	0.69	0.80	—	0.53
20-Oxo-7a-aza-B-homopregn-5-eno[7a,7-*d*]tetrazol-3β-ol[21,28,29]	0.27	0.49	0.47	0.44	0.28	—	0.19
20-Oxo-7a-aza-B-homo-5α-pregnano[7a,7-*d*]tetrazol-3β-ol[29]	0.26	0.41	0.47	0.35	0.29	—	0.19
7a-Aza-B-homopregn-4-eno[7a,7-*d*]tetrazole-3,20-dione[28,29]	0.55	0.75	0.66	0.72	0.74	—	0.43
7a-Aza-B-homo-5α-pregnano[7a,7-*d*]tetrazole-3,20-dione[29]	0.54	0.58	0.56	0.50	0.71	—	0.35
3β-Hydroxy-7a-aza-B-homoandrost-5-eno[7a,7-*d*]-tetrazol-17β-yl acetate[28,29]	0.28	0.53	0.50	0.56	0.30	—	0.33
3-Oxo-7a-aza-B-homoandrost-4-eno[7a,7-*d*]tetrazol-17β-yl acetate[28,29]	0.83	0.74	0.55	0.78	0.72	—	0.42
7a-Aza-B-homoandrost-5-eno[7a,7-*d*]tetrazole-3β,17β-diol[29]	0.11	0.44	0.39	0.29	0.13	—	0.20
3-Oxo-7a-aza-B-homoandrost-4-eno[7a,7-*d*]tetrazol-17β-ol[28,29]	0.18	0.37	0.38	0.31	0.25	—	0.20
17β-Acetamido-7a-aza-B-homoandrost-5-eno-[7a,7-*d*]tetrazol-3β-yl acetate[21]	—	0.43	0.42	0.32	0.31	—	0.21
17β-Acetamido-7a-aza-B-homoandrost-5-eno-[7a,7-*d*]tetrazol-3β-ol[21]	0.07	0.20	0.35	0.19	0.09	—	0.10
17β-(5-Methyltetrazol-1-yl)-7a-aza-B-homoandrost-5-eno[7a,7-*d*]tetrazol-3β-yl acetate[21]	0.52	0.51	0.52	0.46	0.57	—	0.21
17β-(5-Methyltetrazol-1-yl)-7a-aza-B-homoandrost-5-eno[7a,7-*d*]tetrazol-3β-ol[21]	0.13	0.19	0.41	0.33	0.18	—	0.07

chloride–methanol (19:1); (16) chloroform–methanol (47:3); (17) *n*-hexane–ethyl acetate–methanol (5:4:1); (18) chloroform–methanol (49:1); (19) benzene–ethyl acetate (1:1); (20) toluene–methanol (17:3); (21) chloroform-ethyl acetate (5:3); (22) *n*-hexane–ethyl acetate–methanol (20:19:1); (23) benzene–methanol (19:1).

RESULTS

Table I lists the R_F values of some steroids used as starting materials and ketones, Table II those of steroidal ketoximes, Table III those of steroidal amides and lactams and Tables IV and V those of steroidal tetrazoles.

TABLE V

R_F VALUES OF STEROIDAL TETRAZOLES IN SOLVENT SYSTEMS 18–23

Compound	*Solvent system*					
	18	*19*	*20*	*21*	*22*	*23*
3-Aza-A-homocholest-4a-eno[3,4-*d*]tetrazol-6-one[30]	0.62	0.63	0.48	0.58	0.70	0.58
(25*R*)-3-Aza-A-homospirost-4a-eno[3,4-*d*]tetrazol-6-one[31]	0.48	0.51	0.41	0.44	0.55	0.40
3-Aza-A-homopregna-4a,16-dieno[3,4-*d*]tetrazole-6,20-dione[31]	0.41	0.38	0.34	0.33	0.32	0.34
3-Aza-A-homoandrost-4a-eno[3,4-*d*]tetrazole[26]	0.63	0.59	0.47	0.56	0.63	0.56
6-Aza-B-homo-5α-cholestano[6,7-*d*]tetrazol-3β-yl acetate[26]	0.67	0.58	0.51	0.56	0.68	0.60
3,6-Diaza-A,B-bishomocholest-4a-eno[6,7-*d*]tetrazol-4-one[31]	0.24	0.62	0.33	0.58	0.67	0.31
7a-Aza-B-homocholest-5-eno[7a,7-*d*]tetrazol-3β-yl acetate[32]	0.61	0.55	0.46	0.54	0.64	0.54
(25*R*)-7a-Aza-B-homospirost-5-eno[7a,7-*d*]tetrazol-3β-yl acetate[28,29]	0.51	0.47	0.41	0.41	0.55	0.44
20-Oxo-7a-aza-B-homo-5α-pregnano[7a,7-*d*]tetrazol-3β-yl acetate[29]	0.43	0.44	0.33	0.34	0.31	0.30
7a-Aza-B-homoandrost-5-eno[7a,7-*d*]tetrazole-3β,17β-diol diacetate[28,29]	0.48	0.40	0.37	0.37	0.42	0.39
(25*R*)-12a-Aza-C-homo-5α-spirostano[12a,12-*d*]tetrazol-3β-yl acetate[33]	0.59	0.54	0.47	0.60	0.58	0.46
20-Oxo-12a-aza-C-homo-5α-pregn-16-eno[12a,12-*d*]-tetrazol-3β-yl acetate[33]	0.33	0.35	0.29	0.33	0.26	0.26
3,6-Diaza-A,B-bishomocholest-4a-eno[3,4-*d*] [6,7-*d*]bis-tetrazole[30]	0.62	0.57	0.45	0.53	0.66	0.53
4,6-Diaza-A,B-bishomocholest-4a-eno[4,3-*d*] [6,7-*d*]bis-tetrazole[31]	0.59	0.66	0.52	0.61	0.63	0.55
3,7-Diaza-A,B-bishomocholest-4a-eno[3,4-*d*] [7,6-*d*]bis-tetrazole[31]	0.37	0.52	0.37	0.43	0.55	0.33
3,7a-Diaza-A,B-bishomocholest-5-eno[3,4-*d*] [7a,7-*d*]bis-tetrazole[24,27]	0.52	0.12	0.29	0.12	0.14	0.14

For the steroidal ketones, consistent results were obtained with solvent systems 1–6 (Table I), of which systems 3 and 4 are particularly useful. Of the solvent systems useful for the ketoximes (5, 7, 8 and 9) (Table II) systems, 5 and 7 are to be preferred. For the steroidal amides and lactams, solvent systems 10, 11, 12, 13, 14 and 15 (Table III), particularly 11, 12 and 14, were useful. Of the several solvent systems (10, 11, 12, 13, 15, 16, 17, 18, 19, 20, 21, 22 and 23) tried for steroidal tetrazoles (Tables IV and V), systems 12 and 17 (Table IV) and 19, 22 and 23 (Table V) gave better results.

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