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Research Article

Rf VALUES OF SOME STEROIDAL KETONES, OXIMES, AMIDES AND LACTAMS IN VARIETY OF SOLVENT SYSTEMS

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Abstract

Bisonium salts of suitable constitution tend to show a high specificity for neuromuscular junction and high potency as neuromuscular blockers. This is a fundamental requisite around which nearly all the rational approaches to synthesize new neuromuscular blockers should be based.

It was seen that bisquaternary structure is more selective for nicotinic sites and where interonium distance is of the order of ≈1 nm, it tends to confine its activity at neuromuscular junction. The identification of unknown compounds is an important task of the organic chemist. Chromatography can be used to support a compound's identification if its chromatographic properties are compared with those of known compounds. Thin-layer chromatography (TLC) is a very commonly used technique in synthetic chemistry for identifying compounds, determining their purity and following the progress of a reaction. It also permits the optimization of the solvent system for a given separation problem. In comparison with column chromatography, it only requires small quantities of the compound (~ng) and is much faster as well.

Different compounds can have the SAME Rf value for a particular solvent, but unlikely to have similar Rf for a number (2-4) of different solvents. Therefore the more different solvents (or mixtures) are used, the more Rf values are obtained, and so the more concise the identification is.

Keywords: Azasteroids, Rf value, Solvent system, Thin layer chromatography.

1. Introduction

The steroid system, selected by the evolutionary process to perform some of the most fundamental biological

functions, has not only inspired the biochemists and endocrinologists, but has also become the basis of the most phenomenal developments in organic chemistry. The broad spectrum of biological activity with in the group and multiplicity of actions, displayed by certain individual members, make the steroid one of the most intriguing classes of biologically active compounds. Therefore, steroidal modification has been of considerable interest to medicinal chemists. The area is also fascinating to the organic chemists, as the preparative work itself is a challenge and also for the study of reaction mechanism and stereochemistry, the steroidal nucleus provides a good base. The heterosteroids constitute a class of modified steroids, which has attracted a considerable attention.

The introduction of Neuromuscular Blocking Agents represents one of the most important advances in anaesthesia and surgery. During these years, research in the area of neuromuscular blocking agents arose dramatically, driven mainly by the quest to find ideal muscle relaxants.

In an on-going programme of studies on azasteroids, a number of azasteroidal compounds of potential medicinal interest have been synthesized. Earlier, results of TLC studies on a variety of steroidal derivatives such as oximes, lactams, ketones, mono-, bis-, and quaternary ammonium compounds and tetrazoles have been published[1-4]. Continuing the programme, in the present communication, we give the TLC results of the compounds hitherto unreported.

2. Experimental:

2.1 Steroidal derivatives: A number of steroidal compounds were mainly prepared in our laboratory (Table I-III). Literature references to the method of preparation of the compounds are given in the tables.

2.2 Adsorbent and TLC plates: Precoated plates (20X20 cm) with Silica gel 60 f_{254} Merck Darmstadt, Germany were used. The running distance was 10 cm at temperature of 22-25^0 and the load of steroidal derivative applied was 50-100 µg.

2.3 Detection: Cerium (IV) sulphate solution [2g in 100ml of 10%(v/v) sulfuric acid] was used as spray reagent (followed by heating) at 150^0 for 30 min, which produced permanent black spots. Exposure to iodine vapours was done which produced brown spots in only 2-4 minutes.

2.4 Solvents: All the solvents were of analytical grade and were used without further treatment. The following solvent systems were used: (1) Benzene: methanol (8:2); (2) Chloroform: methanol (9:1); (3) Chloroform: methanol: ethyl

acetate (8:2:10). (4) Benzene: methanol: ethyl acetate (15:3:2); (5) Methanol: acetic acid: water (7:1:2); (6) Methanol: acetic acid: water (4.5:0.5:5); (7) Methanol: acetic acid: ethyl acetate (4.5:0.5:5).

3. Results and Discussion:

Table I to III list the R_f values of the steroidal compounds synthesised.

Table-I: Thin-Layer Chromatography of Steroidal Oximes and Alcohols in Solvent Systems 1,2,3,4 and 7.

Compound	*R_f values*				
	1	2	3	4	7
20-Oximino-5,16-pregnadien-3β-yl acetate[5,6,7]	0.62	0.76	0.79	0.69	0.82
17-Oximino-5-androsten-3β-yl acetate[8]	0.50	0.62	0.76	0.66	0.74
17a- Aza-D-homo -5-androsten-3β-ol[10]	0.38	0.39	0.67	0.46	0.55

Table II: Thin-Layer Chromatography of Steroidal Ketones in Solvent Systems 1,2,3,4 and 7.

Compound	*R_f values*				
	1	2	3	4	7
17-Oxo-5-androsten-3β-yl acetate[11]	0.72	0.69	0.73	0.70	0.75
17-Oxo-17a-aza-D-homo-5-androsten-3β-yl acetate[12,13]	0.43	0.41	0.50	0.43	0.75
17a-Aza-D-homo-5-androsten-3-one[14,15]	0.62	0.94	0.96	0.70	-
17a-(Hydroxy ethyl) -17a-aza-D-homo-androsten-3-one[16]	0.71	0.96	0.94	0.71	-
17a-Allyl-17a-aza-D-homo-5-androsten-3-one	0.61	0.72	0.95	0.56	-

Table III: Thin layer chromatography of Mono, Di and Triaza steroidal compounds in solvent system 1,2,3,4,5,6 and 7.

Compound	*R_f Values*						
	1	2	3	4	5	6	7
17a-(Hydroxyethyl)-4-methyl-3-piperidin-1-ylidinium-17a-aza-D-homo-5-androstene dimethiodide	0.18	0.25	0.30	0.25	0.97	0.93	0.80
17a-(Acetoxy ethyl)-4-methyl-3-piperidin-1-ylidinium-17a-aza-D-homo-5-androstene dimethiodide	0.27	0.52	0.45	0.23	1	0.96	0.84
17a-Allyl-4-methyl-3-piperidin-1-ylidinium-17a-aza-D-homo-5-androsten dimethiodide[11]	0.52	0.37	0.31	0.31	1	0.57	0.72
17a-Allyl-3β -piperazino-17a-aza-D-homo-3,5-androstadiene [10]	0.30	0.68	0.28	0.43	0.86	-	-
17a-Allyl-3β -piperazino-17a-aza-D-homo-5-androstene trimethiodide [8,17,22]	0.46	0.75	0.50	0.45	1	0.55	0.89
3β-Quinolino-17a-aza-D-homo-androst-3,5-diene-17-one [9,10]	0.50	0.64	0.62	0.53	0.71	-	-
3β-Quinolino-17a-aza-D-homo-5-androsten-17-one [18]	0.36	0.96	0.58	0.57	1	-	-
3β-Quinolino-17a-aza-D-homo-5-androstene	0.40	0.18	0.13	0.17	1	-	-
17a-(2-Hydroxyethyl) -3β- quinolino-17a-aza-D-homo-5-androstene [16]	0.39	0.40	0.44	0.38	0.83	-	-
17a-(2-Hydroxyethyl) -3β- quinolino-17a-aza-D-homo-5-androsten dimethiodide [10]	0.33	0.67	0.38	0.56	0.91	0.60	0.86
17a-(2-Acetoxyethyl) -3β- quinolino-17a-aza-D-homo-5-androsten dimethiodide [10]	0.59	0.74	0.67	0.63	1	0.60	0.84
17a-Allyl-3β- quinolino-17a-aza-D-homo-5-androstene [12]	0.51	0.60	0.56	0.55	1	-	-
17a-Allyl-3β- quinolino-17a-aza-D-homo-5-androsten dimethiodide [11,13]	0.34	0.72	0.56	0.29	1	0.58	0.93

17a-Ethyl-3β-quinolino-17a-aza-D-homo-5-androstene [12]	0.63	0.60	0.33	0.34	0.91	-	-
17a-Ethyl-3β-quinolino-17a-aza-D-homo-5-androsten dimethiodide [10]	0.44	0.61	0.50	0.44	0.60	0.62	0.09
17a-Allyl-3β-morpholino-17a-aza-D-homo-5-androstene dimethiodide [19,20,21]	0.94	0.23	0.10	0.08	0.09	0.10	0.89
17a-Allyl-3β-piperidino-17a-aza-D-homo-5-androstene trimethiodide [10,12]	0.62	0.90	0.78	0.63	0.98	0.65	0.78
3β- Piperidino-17a-aza-D-homo-5-androstene [10,21]	0.56	0.71	0.51	0.55	0.10	0.74	0.77
17a-(2-Acetoxyethyl)- 3β-(1-piperidino)-17a-aza-D-homo-5-androsten dimethiodide[10,16]	0.58	0.75	0.56	0.53	1	0.83	0.81

4. Conclusion:

For steroidal oximes consistent results were obtained with solvent systems 3 and 4 (Table I). For steroidal 3-oxo compounds solvent system 3 was of particular interest (Table II) whereas for 17-oxo steroidal compounds solvent system 7 is to be preferred (Table II). Compounds having 17-hydroxyethyl and 17-acetoxyethyl moieties gave consistent results in solvent system 7 (Table III) of the solvent systems used for bisquaternary steroidal compounds having 17a-allyl substitition, solvent system 6 is to be prefered.

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