PAPER CHROMATOGRAPHY OF AZAADAMANTANE DERIVATIVES*

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Received November 30th, 1973

Paper chromatography was studied in various solvent systems of 1-azaadamantane and its quaternary salts, of 1,3-diazaadamantane and its tetrasubstituted derivatives, and of 1,3,5-triazaadamantane and its derivatives.

Literature lacks studies on paper chromatography of azaadamantanes. We focused our attention on this problem and studied compounds synthetized in our laboratory earlier from this viewpoint. The solvent systems used are summarized in Table I, the results are given in Tables II–IV.

TABLE I
Solvent Systems

Designation	System	Composition
S_1	2-propanol–hydrochloric acid–water	20 : 1 : 2
S_2	2-methyl-1-propanol–hydrochloric acid–water	20 : 1 : 2
S_3	butanol saturated with water	
S_4	butanol–acetic acid–water	4 : 1 : 5
S_5	2-propanol–acetic acid–water	4 : 1 : 2
S_6	butanol–acetic acid–water	4 : 1 : 2
S_7	ethanol–ammonia (25%)–water	20 : 1 : 4
S_8	methanol–water	10 : 1
S_9	ethanol–water	10 : 1
S_{10}	butanol–ethanol–water	4 : 1 : 1

The chromatography of 1-azaadamantane and of its quaternary salts was studied in solvent systems containing hydrochloric acid. In these systems, a satisfactory separation of the homologous series of quaternary salts can be achieved, similarly

* Part IV in the series Nitrogen Compounds of Adamantane; Part III: This Journal *39*, 895 (1974).

to pyridine bases[1]. An especially effective resolution was obtained in systems containing an alcohol with a branched chain, such as 2-propanol or 2-methyl-1-propanol. The Dragendorff reagent[2] was used for the detection.

Tetrasubstituted derivatives of 1,3-diazaadamantane cannot be resolved satisfactorily in solvent systems containing hydrochloric acid and the individual components remain at the origin. Hydrochloric acid was therefore replaced by acetic acid in these systems. The best of all systems tested, however, is system S_7 containing ammonia.

TABLE II

R_F-Values of 1-Azaadamantane and its Quaternary Salts

Compound	S_1	S_2	S_3	S_4
1-Azaadamantane	0·39	0·39	0·29	0·48
1-Methyl-	0·34	0·27	0·29	0·52
1-Ethyl-	0·39	0·35	0·31	0·56
1-Propyl-	0·64	0·56	0·41	0·67
1-Isopropyl-	0·44	0·41	0·35	0·64
1-Butyl-	0·76	0·73	0·55	0·72
1-Pentyl-	0·89	0·77	0·64	0·78
1-Hexyl-	—	0·80	0·74	0·86
1-Allyl-	0·54	0·50	0·36	0·59
1-Benzyl-	0·71	0·73	0·51	0·73
1-Hydroxyethyl-	0·36	0·29	0·22	0·48
1-(2-Bromoethyl)-	0·49	0·49	0·38	0·64
1-(6-Bromohexyl)-	0·90	0·77	0·67	0·82

TABLE III

R_F-Values of 1,3-Diazaadamantane and its Derivatives

Compound	S_5	S_6	S_7
1,3-Diazaadamantane	0·71	0·42	0·79
2,4,6,8-Tetra(3-pyridyl)-3,7-diazabicyclo[3,3,1]nonan-9-one	0·75	0·56	0·75
2,4,6,8-Tetra(3-pyridyl)-3,7-diazabicyclo[3,3,1]nonan-9-ol	0·77	0·54	0·75
4,8,9,10-Tetra(3-pyridyl)-1,3-diazaadamantane-6-one	0·72	0·56	0·69
4,8,9,10-Tetra(3-pyridyl)-3,7-diazaadamantane-6-ol	0·76	0·53	0·80
2,6-Di(3-pyridyl)piperidin-4-ol	0·72	0·49	0·77

The Dragendorff reagent was used again for the detection. It is especially useful for derivatives containing a pyridine ring in their molecules, which are stained red.

The Dragendorff reagent could not be used for the detection of 1,3,5-triazaadamantane and its derivatives in certain cases. Compounds which do not contain either a primary or a secondary amino group in their molecules (such as, *e.g.* 7-nitro-, 7-chloro- or 7-bromo-1,3,5-triazaadamantane) and which thus are weaker bases, react unsatisfactorily with this reagent and give very little visible spots. A solution of 4-dimethylaminobenzaldehyde in ethanol and hydrochloric acid[2] was used for the detection of these types of compounds. Yellow spots are obtained after the chromatogram has been dried at 150°C. Spraying with a 1% solution of bromocresol green in ethanol, which stains the compounds blue in a neutral medium, was used in other cases. Therefore neutral solvent systems were mostly chosen.

EXPERIMENTAL

The melting points are not corrected.

Compounds Used

1-Alkyl-1-azoniaadamantane bromides: 1-Azaadamantane was prepared according to paper[3]. The quaternary salts were prepared by the reaction of 1-azaadamantane with the corresponding alkyl

TABLE IV

R_F-Values of 1,3,5-Triazaadamantane and its Derivatives

Compound	S_3	S_6	S_8	S_9	S_{10}
1,3,5-Triazaadamantane	0·20	0·40	0·50	0·41	0·36
7-Nitro-	0·54	—	0·64	0·52	0·55
7-Amino-	0·21	0·39	0·39	0·25	0·17
7-Chloro-	0·68	0·64	0·73	0·62	0·68
7-Bromo-	0·70	0·66	0·71	0·63	0·70
7-Benzylamino-	0·62	0·62	0·57	0·50	0·61
7-[(4-Dimethylamino)benzylamino]-	0·60	0·57	0·54	0·48	0·56
7-(Cyanomethyl)amino-	0·22	0·42	0·43	0·30	0·24
7-Hydroxylamino-	0·23	0·41	0·37	0·24	0·17
7-(Aminoethyl)amino-	0·09	0·26	0·23	0·10	0·09
7-[(4-Chlorobenzyl)amino]-	0·72	0·75	0·60	0·56	0·62
7-[(4-Methoxybenzyl)amino]-	0·59	0·66	0·57	0·47	0·47
7-[(4-Picolyl)amino-	0·33	0·44	0·41	0·29	0·30
7-(3-Picolyl)amino-	0·31	0·40	0·38	0·27	0·29
7-Butylamino-	0·57	0·61	0·66	0·60	0·43
N-Phenyl-N′-[7-(1,3,5)-triazaadamantyl)]urea	0·80	0·85	0·73	0·78	0·79
7-Nitro-1,3,5-triazaadamantane-N-oxide	0·27	0·55	0·53	0·31	0·26

halogenides (bromides, unless stated otherwise). The following preparations were synthetized: 1-methyl-(iodide, m.p. > 400°C, decomp.); 1-ethyl- (m.p. > 400°C, decomp.); 1-propyl- (m.p. > > 400°C, decomp.); 1-isopropyl- (m.p. > 400°C decomp.); 1-butyl- (m.p. > 400°C, decomp.); 1-pentyl- (m.p. 318—320°C); 1-hexyl- (m.p. 298—300°C); 1-allyl- (m.p. 284—285°C); 1-benzyl-(chloride, m.p. 342—344°C); 1-hydroxyethyl-(chloride, m.p. > 400°C, decomp.); 1-(2-bromoethyl)- (m.p. 246—247°C); 1-(6-bromohexyl)- (m.p. 200—201°C).

1,3-Diazaadamantane was prepared by the method described in paper[4]. The reactions described in paper[5] were used for the preparation of the following compounds: 2,4,6,8-tetra(3-pyridyl)--3,7-diazabicyclo[3,3,1]nonan-9-one (m.p. 252—253°C); 2,4,6,8-tetra(3-pyridyl)-3,7-diazabicyclo-[3,3,1]nonan-9-one (m.p. 313—314°C); 4,8,9,10-tetra(3-pyridyl)-1,3-diazaadamantane-6-on (m.p. 290—291°C); 4,8,9,10-tetra(3-pyridyl)-1,3-diazaadamantane-6-ol (m.p. 302—303°C); 2,6-di(3--pyridyl) piperidin-4-ol (m.p. 204—205°C).

1,3,5-Triazaadamantane was prepared as described in paper[6]. The reactions described in the study[6] cited were used for the preparation of the following 1,3,5-triazaadamantane derivatives: 7-nitro-(m.p. 300—302°C, in sealed capillary tube); 7-amino-(m.p. 303—305°C, in sealed capillary tube); 7-chloro-(m.p. 224—225°C, in sealed capillary tube); 7-bromo- (m.p. 217—218°C, in sealed capillary tube); 7-benzylamino- (m.p. 213—214°C); 7-[(4-dimethylamino)benzylamino]-(m.p. 216—217°C); 7-(cyanomethyl)amino- (m.p. 157°C); 7-hydroxylamino-(m.p. 228°C); 7-(aminoethyl]amino- (m.p. 101—102°C); 7-[(4-chlorobenzyl)amino]- (m.p. 170—171°C); 7-[(4-methoxybenzyl)amino]- (m.p. 180—181°C); 7-(4-picolyl)amino- (m.p. 210—211°C); 7-(3-picolyl)amino-(m.p. 188—189°C); 7-butylamino- (m.p. 103—104°C); N-phenyl-N'[7-(1,3,5-triazaadamantyl)] urea (m.p. 202°C, decomp.); 7-nitro-1,3,5-triazaadamantane-N-oxide (m.p. 214—215°C).

Chromatography

Descending chromatography on Whatman No 1 paper was used. The chromatography was carried out at 20°C; the samples applied contained 0·01—0·02 of compound in 1 ml of solution. The quaternary salts of 1-azaadamantane and 1,3,5-triazaadamantane derivatives were applied as aqueous solutions. The derivatives of 1,3-diazaadamantane were dissolved in acetic acid or in a mixture of ethanol and hydrochloric acid. The results are given in Tables I—IV.

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Translated by V. Kostka.