

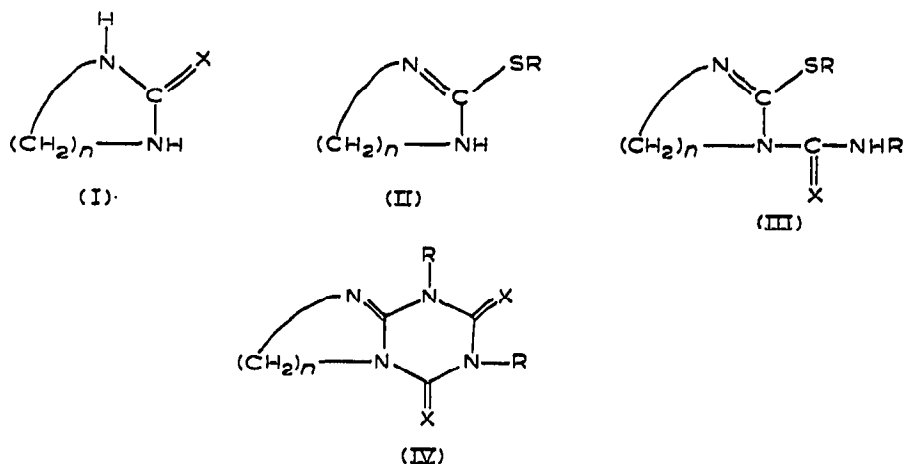
CHROMATOGRAPHIC BEHAVIOUR OF UREAS, THIOUREAS, BIURET DERIVATIVES AND RELATED COMPOUNDS

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In the course of an investigation on the influence of geometrical, electronic and other factors on the formation and reactivity of non-aromatic heterocycles^{1,2}, we obtained and studied several types of compounds, which are represented by the general formulae I-IV:



In this paper we describe conditions suitable for the separation and chromatic detection of the various compounds. This work has been of considerable aid in the separation and identification of the above products and has provided in several cases a simple and rapid method of following the progress of a reaction.

EXPERIMENTAL

Materials and method

Silica Gel G: E. Merck A.G., Darmstadt.

Spreader and chromatography tanks: Desaga GmbH, Heidelberg.

Solvents: Merck, Fluka, Erba, specially prepared for chromatography.

Thickness of the layer: 250 μ .

The coated plates were dried at room temperature overnight.

The samples were dissolved in anhydrous methanol or acetone and applied by following the usual procedures³. The ascending technique was used and the solvent front was allowed to reach 10 cm, keeping the volume of the solvent systems always

constant. Saturation of the tank atmosphere was of particular importance for the reproducibility of results⁴.

The solvent systems used were:

- (A) Ethyl acetate-methanol (50:50)
- (B) Ethyl acetate-benzene (60:30)
- (C) Ethanol-ammonium hydroxide 25 % (80:20)
- (D) Chloroform-acetone-diethylamine (50:40:10)
- (E) Chloroform-methanol (95:5)
- (F) Ethyl acetate-pyridine (70:20)

Times required for separations under the given conditions were: (A) 10 min; (B) 12 min; (C) 55 min; (D) 13 min; (E) 10 min; (F) 20 min; respectively.

Each R_F value is the arithmetical mean of twelve separate measurements.

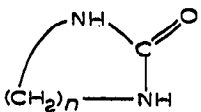
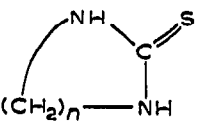
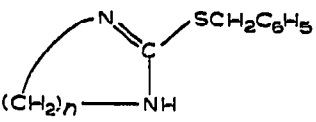
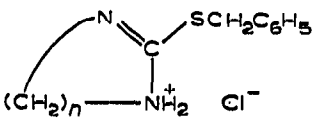
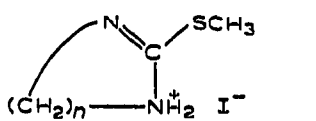
Detection

GROTE's reagent⁵. The reaction is attributed to the formation of complexes between the pentacyanoaquoferrate ions and compounds containing $>C=S$ or $\geq C-SR$ groups. Such complexes are strongly colored and have sufficient stability.

TABLE I

R_F VALUES $\times 100$ AND COLORS OBSERVED WITH ISOTHIOURONIUM BASES AND SALTS, THIOUREAS AND UREAS

Colors, developed at room temperature: B = blue; Bn = brown; Bn-V = brown violet; G = green; Gr = grey; Y = yellow; Rs = rose; W = colorless on the colored background; V = violet.

	n	Solvent systems (see text)				Chromatic reactions		
		A	B	C	D	Grote	Feigl	Cl_2-I_2
	2	10	—	75	18	—	Y	Bn
	3	5	—	74	14	—	Y	Bn
	4	13	—	80	33	—	Y	Bn
	2	40	12	69	32	B	W	Bn
	3	31	7	76	40	B	W	Bn
	4	48	25	82	56	B	W	Bn
	2	—	—	5	43	V	Y	Bn
	3	—	—	4	42	—	Y	Bn
	4	—	—	10	57	—	Y	Bn
	2	—	—	84	63	V	Y	Bn
	3	—	—	72	62	—	Y	Bn
	4	—	—	78	70	—	Y	Bn
	2	—	—	74	51	V	Y	Bn
	3	—	—	53	43	—	Y	Bn
	4	—	—	51	61	—	Y	Bn

Their formation is apparently facilitated by moderate heating, whereas at a higher temperature they are destroyed⁶.

FEIGL's reagent⁷. This reaction is based on the ability of sulfur-containing compounds to catalyse the oxidation of the azide ion by iodine. Colorless spots on a brown background are observed. They could subsequently be made more evident by spraying a dilute solution of starch on the plate. In many cases brown or yellow spots were observed whose nature has not been elucidated.

*Chlorine-iodine reagent*⁸. This reagent allowed the detection of all compounds.

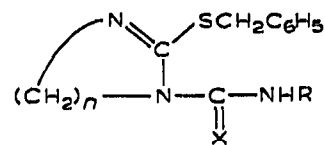
Among the chromatic reagents used the $\text{Cl}_2\text{-I}_2$ was found to be most sensitive. With the first two reagents it was possible to show up 1-2 μg of each compound, while with the third reagent as little as 0.5 μg could be detected.

RESULTS AND DISCUSSION

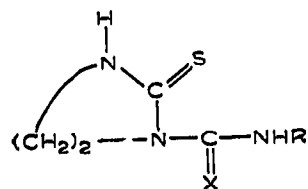
In Table I, the R_F values and colors observed with some isothiuronium bases, isothiuronium salts, thioureas and ureas are reported. A comparison of the chromatic

TABLE II

R_F VALUES $\times 100$ OF ISOTHIABIURET DERIVATIVES AND CORRESPONDING THIABIURETS



R	X	n	R_F values $\times 100$ in solvent systems				Detection		
			A	B	E	F	Grote	Feigl	$\text{Cl}_2\text{-I}_2$
C_6H_5	O	2	—	—	46	42	V	W	Bn
C_6H_5	S	2	—	—	51	62	BG	W	Bn
$\text{C}_6\text{H}_4\text{NO}_2$	S	2	—	—	50	64	G	W	Bn
$\text{C}_6\text{H}_4\text{N}(\text{CH}_3)_2$	S	2	—	—	59	60	Gr-G	W	Bn
CH_3	S	4	—	—	67	70	B-G	W	Bn



R	X	R_F values $\times 100$ in solvent systems				Detection		
		A	B	C	D	Grote	Feigl	$\text{Cl}_2\text{-I}_2$
C_6H_5	O	58	33	77	32	—	W	Bn
C_6H_5	S	64	53	81	40	Rs-V	W	Bn
$\text{C}_6\text{H}_4\text{NO}_2$	S	61	45	82	32	Bn-Rs	Bn	Bn
$\text{C}_6\text{H}_4\text{N}(\text{CH}_3)_2$	S	61	52	83	44	Bn-V	Bn	Bn

reactions shows that in general, the same color develops in connection with a functional group, independent of whether it is included in a five, six or seven-membered ring. This is not true for the five-membered ring isothiurea which forms a violet complex with GROTE's reagent, while the six- and seven-membered analogs do not react appreciably. This fact suggests that the influence of the geometry of the ring may have a bearing on the formation of complexes, as well as in the reactions with dipolarophiles^{1,2}.

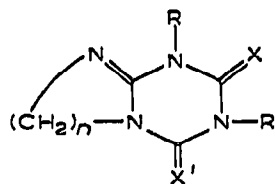
Table II shows the chromatographic behaviour of isothiobiuret derivatives and of corresponding thiobiurets.

Table III deals with some new derivatives of the heterocyclic systems imidazo-, pyrimido- and diazepino-triazines and products obtained upon their degradation. An X-ray investigation has confirmed the structure of one of these compounds⁹.

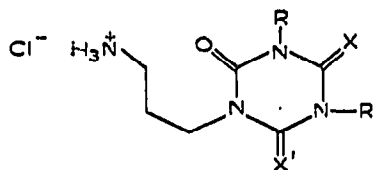
In Table IV the R_F values of some iso(thio)cyanates and acyclic thiureas are given for comparison. The use of anhydrous solvents is of fundamental importance for

TABLE III

R_F VALUES $\times 100$ OF DERIVATIVES OF IMIDAZO-, PYRIMIDO- AND DIAZEPINO-TRIAZINES



n	R	X	X'	Solvent systems				Detection		
				A	B	C	D	Grote	Feigl	Cl ₂ -I ₂
2	C ₆ H ₅	S	S	58	32	84	69	—	W	Bn
	C ₆ H ₄ NO ₂	S	S	64	34	87	67	—	W	Bn
3	CH ₃	S	S	64	54	86	68	—	W	Bn
	CH ₃	S	O	55	32	84	63	—	B-V	Bn
	C ₆ H ₅	S	S	65	53	84	70	—	W	Bn
	C ₆ H ₄ NO ₂	O	O	45	17	81	66	—	Br	Bn
4	C ₆ H ₄ NO ₂	S	S	68	55	86	69	G	W	Bn
	C ₆ H ₅			67	58	87	66	—	W	Bn
	C ₆ H ₄ NO ₂			72	61	81	66	—	Br	Bn

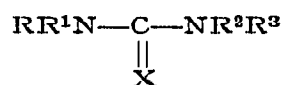


R	X	X'	Solvent systems				Detection		
			A	B	C	D	Grote	Feigl	Cl ₂ -I ₂
CH ₃	S	S	—	—	82	68	B	W	Bn
CH ₃	S	O	—	—	64	63	—	V	Bn

TABLE IV

R_F VALUES \times 100 OF SOME ISOTHIOCYANATES AND ACYCLIC THIOUREAS
R-NCX

R	X	Solvent systems				Detection		
		A	B	E	F	Grote	Feigl	Cl ₂ -I ₂
CH ₃	S	63	58	57	71	—	W	Bn
C ₆ H ₅	S	60	65	65	79	—	W	Bn
C ₆ H ₅	O	64	59	58	—	—	Bn	Bn
C ₆ H ₄ NO ₂	S	71	62	61	80	—	Y	Bn
C ₆ H ₄ N(CH ₃) ₂	S	65	62	70	68	B-G	Bn-V	Bn



R	R ¹	R ²	R ³	X	Solvent systems				Detection		
					A	B	C	D	Grote	Feigl	Cl ₂ -I ₂
C ₆ H ₅	H	H	C ₆ H ₅	O	63	59	86	33	B	W	Bn
CH ₃	H	H	H	S	36	10	81	12	B	W	Bn
CH ₃	H	CH ₃	CH ₃	S	42	24	88	52	B	W	Bn
CH ₃	H	H	CH ₃	S	47	13	85	27	B	W	Bn
CH ₃	CH ₃	CH ₃	CH ₃	S	60	49	93	65	Bn-V	Bn-V	Bn

the development of phenyl isocyanate because of the easy formation of N,N'-diphenylthiourea.

SUMMARY

The separation conditions of some non-aromatic heterocyclic and related compounds are given. Some chromatic reactions used to localize the products are described and briefly discussed.

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