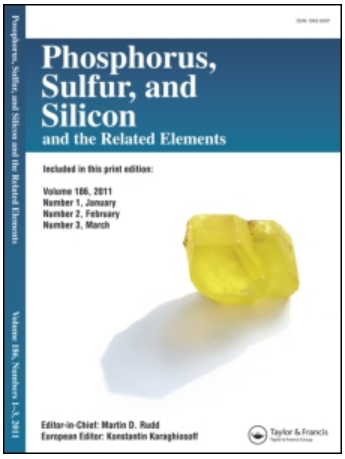

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Thio Analogs of Pyrimidine Bases: Syntheses, EIMS and 13 C NMR Study of New Ortho -(Meta - and Para -) Substituted Derivatives of 2-benzylthio-5-bromo-6-methyluracils

Elżbieta Wyrzykiewicz[a]; Sebastian Mielcarek[a]; Anna Migoń[a]; Jolanta Badura[a]
[a] Faculty of Chemistry, Adam Mickiewicz University, Poznań, Poland

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THIO ANALOGS OF PYRIMIDINE BASES: SYNTHESES, EIMS AND ^{13}C NMR STUDY OF NEW *ORTHO*-(*META*- AND *PARA*-) SUBSTITUTED DERIVATIVES OF 2-BENZYLTHIO-5-BROMO-6-METHYLURACILS

Elżbieta Wyrzykiewicz, Sebastian Mielcarek, Anna Migoń, and Jolanta Badura
Faculty of Chemistry, Adam Mickievicz University, Poznań, Poland

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Nine new ortho-*(*meta- *and* para-*) substituted derivatives of 2-benzylthio-5-bromo-6-methyluracils have been prepared. EI induced mass spectral fragmentation of these compounds was investigated. Fragmentation pathways are proposed on the basis of accurate mass and metastable transitions measurements. The correlation between the intensities of the $M^{+\cdot}$ and the selected fragment ions of these compounds is discussed. ^{13}C NMR spectra of these compounds were assigned. The data derived from EIMS and ^{13}C NMR spectra can be used to differentiate the isomers.*

Keywords: 2-benzylthio-5-bromo-6-methyluracils; ^{13}C NMR; EIMS; *ortho*-(*para*- and *meta*-)chloro-(bromo- and nitro-)benzyl halides; structural isomers

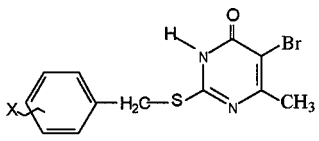
INTRODUCTION

Thio analogs of pyrimidine bases have occupied a unique place and have remarkably contributed to biological and medicinal chemistry. Various analogs of 5-bromo-N-benzyl substituted thiouracils constitute a novel class of centrally acting agents.[1] The pyrimidine thioeters, with 2-benzylthio substituent have been reported to constitute a novel class of non nucleoside HIV-1 reverse transcriptase inhibitors (NNRTI's) with activity against BHAP-resistant HIV.[2,3]

Address correspondence to E. Wyrzykiewicz, Faculty of Chemistry, Adam Mickievicz University, Grunswald 6, 60-780 Poznan, Poland. E-mail: wyrzyk@main.amu.edu.pl

Recently, we have reported the syntheses, physicochemical properties, and results of a mass spectrometric study of 2-*ortho*-(*meta*- and *para*-)chloro-(bromo- and nitro-)benzylthiouracils and 6-methyluracils.[4,5] However, to the best of our knowledge, no work has been published on the synthesis and physicochemical properties of S-benzyl substituted derivatives of 2-thio-5-bromo-6-methyluracils. C-5 bromo group is a hydrofobic substituent having also electronnegative properties, very important for anaesthetic and anti-conflict activities.[1] This fact has stimulated us to prepare a series of 2-*ortho*-(*meta*- and *para*-)chloro-(bromo- and nitro-)benzylthio-5-bromo-6-methyluracils (**1–9**) (Figure 1).

This article deals with the synthesis and physicochemical properties of **1–9**. The analyses of EI mass spectra and ^{13}C NMR spectra of these compounds are connected with differentiation of positional isomers. We wished to establish whether it would be possible to determine the position of halo- (or nitro-) groups in the phenyl ring on the basis of the differences in the values of μ, that is, the ratio of the intensity of the selected fragment ions peaks to that of the parent ion



1 – 9

1 X = *o* – Cl

2 X = *m* – Cl

3 X = *p* – Cl

4 X = *o* – Br

5 X = *m* – Br

6 X = *p* – Br

7 X = *o* - NO_2

8 X = *m* - NO_2

9 X = *p* - NO_2

FIGURE 1 Structures of substituted 2-benzylthio-5-bromo-6-methyluracils **1–9**.

peak, and to compare the data with those previously obtained in our laboratory.[4,5]

RESULTS AND DISCUSSION

A series of nine new *ortho*-(*meta*- and *para*-)chloro-(bromo- and nitro-) substituted 5-bromo-6-methyluracils **1–9** have been synthetized by direct bromination of the appropriate 2-benzylthio-6-methyluracils with bromine in carbon tetrachloride, at room temperature. The treatment of these *ortho*-(*meta*- and *para*-) substituted derivatives of 2-benzylthio-6-methyluracils with the excess of bromine in carbon tetrachloride followed by short boiling of the crude product in ethanol solution, leads to 5-bromo-2-benzylthio-6-methyluracils. The C-5 bromine containing compounds **1–9** were confirmed by examining their UV/VIS, IR and ^{1}H NMR spectra (Table II), as well as elemental analyses (Table I).

The ^{1}H NMR spectra of these compounds show the lack of the characteristic resonances of the protons situated at C-5 of the pyrimidine rings in comparison with the ^{1}H NMR spectra of the substrates,

TABLE I Physical and Analytical Data of Compounds **1–9**

					Analysis Calcul./Found		
Comp.	Formula (m.w)	m.p. (°C)	Yield (%)	R_f TLC	C	H	N
1	$C_{12}H_{10}N_2OSClBr$ (345.64)	220–222	55	0.55	41.73 42.03	2.89 2.69	8.11 8.05
2	$C_{12}H_{10}N_2OSClBr$ (345.64)	198–200	56	0.56	41.73 47.00	2.89 2.74	8.11 7.98
3	$C_{12}H_{10}N_2OSClBr$ (345.64)	170–171	61	0.61	41.73 42.07	2.89 2.77	8.11 8.12
4	$C_{12}H_{10}N_2OSBr_2$ (390.09)	214–216	61	0.66	36.92 37.05	2.56 2.28	7.17 7.06
5	$C_{12}H_{10}N_2OSBr_2$ (390.09)	194–196	62	0.69	36.92 36.90	2.56 2.49	7.17 7.01
6	$C_{12}H_{10}N_2OSBr_2$ (390.09)	196–198	60	0.65	36.92 37.14	2.56 2.36	7.17 7.02
7	$C_{12}H_{10}N_3O_3SBr$ (356.18)	238–240	62	0.62	40.45 40.48	2.80 2.65	11.79 11.49
8	$C_{12}H_{10}N_3O_3SBr$ (356.18)	184–186	80	0.63	40.45 40.64	2.80 2.60	11.79 11.54
9	$C_{12}H_{10}N_3O_3SBr$ (356.18)	214–216	82	0.62	40.45 40.61	2.80 2.57	11.79 11.31

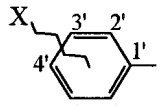
TABLE II IR and UV/VIS Spectral Data of Compounds **1–9**

Compound	IR [cm^{-1}]			UV/VIS	
	ν C$_4$ = O	ν S—CH$_2$	ν C$_5$—Br	λ max [nm]	(lg ε)
1	650	2930	560	296	3.99
				213	4.06
2	1650	2940	550	296	4.00
				214	3.99
3	1660	2940	550	296	4.20
				213	4.01
4	1660	2860	550	296	3.99
				213	4.00
5	1659	2930	560	296	3.99
				212	4.15
6	1660	2850	550	290	4.08
				214	4.02
7	1665	2900	555	291	4.01
				214	4.12
8	1660	2940	560	296	4.01
				214	4.15
9	1665	2940	560	290	4.20
				211	4.13

that is, the appropriate 2-benzylthio-6-methyluracils. The IR spectra of **1–9** show absorption bands of medium intensities in the region 520 cm^{-1}, which have been assigned to ν C-Br vibrations. It has been pointed out that the UV/VIS spectra of **1–9** show λ max in the range 287–296 nm (Table II) and bathochromic shifts as well as increase in absorption in comparison with the corresponding UV/VIS data of *ortho-* (*meta- and para-*)substituted 2-benzylthio-6-methyluracils.[4,6]

The ^{1}H and ^{13}C NMR data of **1–9** are given in Tables III and IV. Assignments of the ^{1}H NMR and ^{13}C NMR resonances of these compounds were deduced on the basis of signal multiplicities, and by the concerted application of two-dimensional NMR techniques ^{1}H, ^{1}H COSY and HETCOR. The HETCOR results allow unequivocal assignment of the ^{13}C NMR spectra, proposed on the basis of the chemical shift theory, additivity rules, and by comparing the measured and the calculated chemical shifts.[7,8] The ^{1}H NMR spectra of **1–9** reveal singlets of S—CH$_2$ and C6—CH$_3$ protons at 4.40–4.60 and 2.44–2.51 ppm respectively. The signals of protons of *ortho-*(*meta-* and *para-*) substituted benzyl groups of **1–9** are seen in the range of 7.18–8.30 ppm (Table III). Table IV gives the ^{13}C NMR data for **1–9**. In order to exemplify the attributions made for each compound on the basis of the analysis of HETCOR spectra, the case of **8** is discussed. For this compound the

TABLE III ^{1}H-NMR Shifts of **1–9**



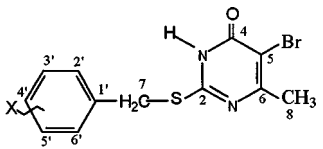
Compound	S—CH_2(s)	C_6—CH_3(s)		
1	4.56	2.48	C-3′ H d 7.73	C-5′ H t 7.25
			C-4′ H t 7.45	C-6′ H d 7.69
2	4.57	2.48	C-2′ H s 7.58	C-5′ H t 7.18
			C-4′ H d 7.40	C-6′ H d 7.30
3	4.60	2.51	C-2′ 6′ H d 7.45	
			C-3′ 5′ H d 7.34	
4	4.42	2.46	C-3′ H d 7.70	C-5′ H t 7.25
			C-4′ H t 7.30	C-6′ H d 7.50
5	4.41	2.46	C-2′ H s 7.50	C-5′ H t 7.20
			C-4′ H d 7.40	C-6′ H d 7.32
6	4.53	2.47	C-2′ 6′ H d 7.50	
			C-3′ 5′ H d 7.40	
7	4.42	2.45	C-3′ H d 8.10	C-5′ H t 7.58
			C-4′ H t 7.71	C-6′ H d 7.90
8	4.52	2.42	C-2′ H s 8.39	C-5′ H t 7.63
			C-4′ H d 8.10	C-6′ H d 7.93
9	4.55	2.46		C-2′ 6′ H d 8.20
				C-3′ 5′ H d 7.80

^{1}H NMR spectrum exhibits three singlets at 13.22 ppm, 4.52 ppm and 2.42 ppm, assigned to N—H, C5—H, and C6—CH_3 of the uracil ring respectively. This spectrum also shows one singlet at 8.39 ppm, two dublets at 8.10 ppm and 7.93 ppm and one triplet at 7.63 ppm assigned to C2′-H, C4′-H, C6′-H, and C5′-H of the phenyl ring respectively.

The correlation between the pair of signals at 135.87 ppm and 122.10 ppm with ^{1}H NMR signals at 7.93 and 8.10 ppm allows the assignment of these signals to C-6′ and C-4′ respectively. Moreover, the triplet at 7.63 in the ^{1}H NMR spectrum due to C-5′H correlates with the signal at 129.71 ppm in the ^{13}C NMR spectrum, as well as the singlet at 8.39 ppm in the ^{1}H NMR spectrum due to C-2′H correlates with the signal at 123.99 ppm in the ^{13}C NMR spectrum. These correlations allow the assignments of these signals to C-5′ and C-2′ respectively. The remaining two carbons at 32.84 and 24.19 ppm are correlated with the singlets of S—CH_2 and C6—CH_3 protons at 4.52 and 2.42 ppm respectively.

A comparison of the number and positions of the signals of the carbon atoms in the ranges of 120–140 ppm (**1–3**) and 120–130 ppm (**4–9**) in

TABLE IV ^{13}C NMR Shifts of **1–9** [a]



1 – 9

C – 2' *ortho*

C – 3' *meta*

C – 4' *para*

Comp.	C-2	C-4	C-5	C-6	C-7	C-8	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′
1	161.73	158.44	107.38	159.99	31.99	24.31	134.27	133.19	129.37	129.28	127.20	131.50
2	161.70	158.46	107.21	159.80	33.11	24.11	139.97	129.04	132.76	127.37	130.27	127.82
3	161.35	158.69	107.35	159.89	32.90	24.20	136.82	130.90	128.10	131.68	128.10	130.90
4	161.71	158.45	107.36	159.90	34.95	24.28	135.91	123.92	132.54	127.76	129.57	131.55
5	161.74	158.47	107.37	160.01	33.05	24.29	140.22	131.95	121.38	130.09	130.50	128.20
6	161.68	158.66	107.10	159.90	33.05	24.24	136.83	131.20	131.25	120.36	131.25	131.21
7	161.71	158.44	107.38	160.02	32.84	24.19	132.51	147.99	124.74	128.90	133.73	133.72
8	161.69	158.44	107.39	159.95	32.84	24.19	140.15	123.99	147.45	122.10	129.71	135.87
9	161.72	158.42	107.38	159.90	32.93	24.13	145.72	130.29	123.35	146.57	123.35	130.29

^{13}C NMR spectra allows a differentiation of isomers *ortho-, meta-* and *para-* substituted in benzylthio groups.

1–3 (Cl substituted isomers)

ortho	*meta*	*para*
C-3′ 129.37 ppm	C-2′ 129.04 ppm	C-3′, 5′ 137.41 ppm
C-4′ 129.28 ppm	C-6′ 127.82 ppm	
C-5′ 127.20 ppm	C-4′ 127.37 ppm	

4–6 (Br substituted isomers)

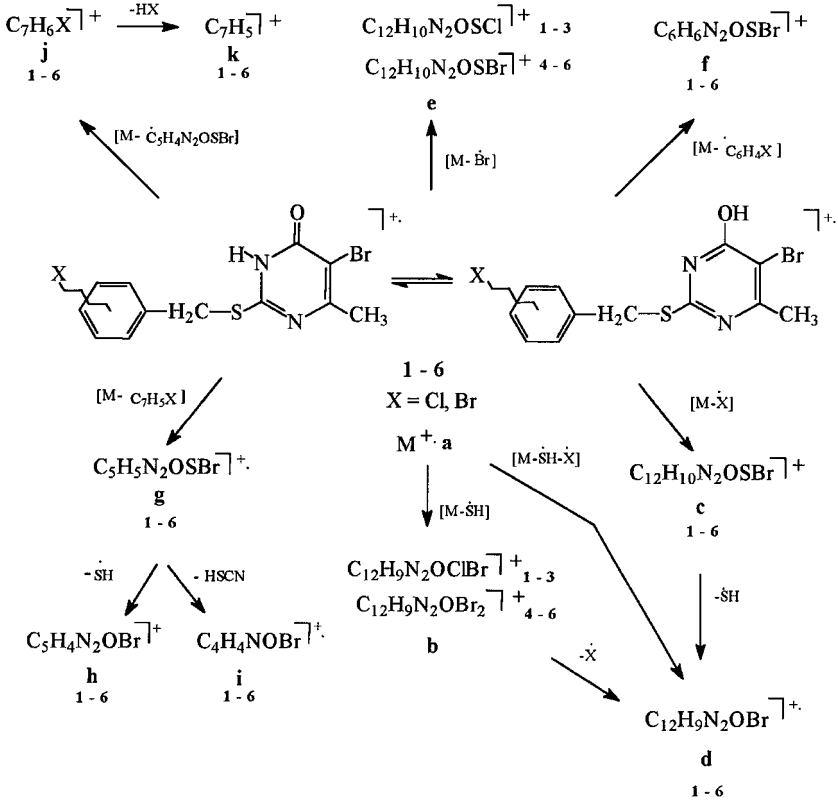
ortho	*meta*	*para*
C-5′ 129.57 ppm	C-6′ 128.20 ppm	C-4′ 120.36 ppm
C-4′ 127.76 ppm	C-3′ 121.38 ppm	
C-2′ 123.92 ppm		

7–9 (NO_2 substituted isomers)

ortho	*meta*	*para*
C-4′ 128.90 ppm	C-5′ 129.71 ppm	C-3′, 5′ 123.35 ppm
C-3′ 124.74 ppm	C-2′ 123.99 ppm	
	C-4′ 122.10 ppm	

As can be seen from Schemes 1 and 2, as well as Tables V and VI, the principal mass fragmentation pathways of the molecular ion of 2-*ortho*-(*meta*- and *para*-)chloro-(bromo- and nitro-)benzylthio-5-bromo-6-methyluracils **1–9** are similar to those of the corresponding 2-*ortho*-(*meta*- and *para*-)chloro-(bromo- and nitro-)benzylthio -6-methyluracils, investigated by us earlier.[4,5] The mass spectra of **1–9** have not revealed the changes in general fragmentation patterns which might have been influenced by the replacement of the hydrogen on C-5 of uracil ring of 2-benzylthio-6-methyluracils with bromine. The common features of the mass spectral fragmentations of the molecular ions of **1–9** are simple inductive cleavages of bonds in the benzylthio substituent, that is, the eliminations of $X^{\cdot}$, $C_6H_4X^{\cdot}$, and $^{\cdot}C_5H_4N_2OSBr$ radicals, giving the even-electron fragment ions **c**, **f**, and **j** respectively. The ejections from the molecular ions of **1–9** of C_7H_5X neutral molecules occur by cleavage of two bonds (Csp^3—S and Csp^2—H) in benzylthio moiety with simultaneous migration of hydrogen from phenyl to uracil ring and formation of odd-electron ions **g**.

It ought to be pointed out that the molecular ions of all compounds investigated readily lose $^{\cdot}SH$ radicals, giving even-electron fragment ions **b**. For this loss to occur, a skeletal rearrangement is required involving cleavage of three bonds (Csp^3—S, Csp^2—S, Csp^3—H) followed by the simultaneous transfer of hydrogen to sulfur atom, elimination of sulphydryl radical and formation of new Csp^3—Csp^2 and Csp^3—N bonds. The even-electron fragment ions **b** which are formed after this rearrangement may have a monocyclic, or bicyclic structure. It should

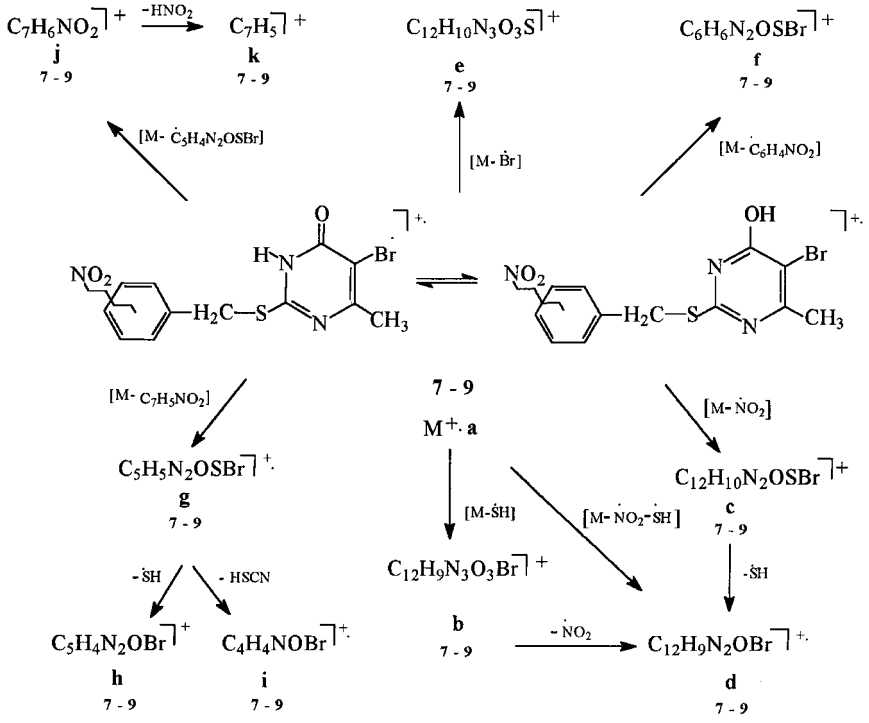


SCHEME 1

be mentioned that loss of a sulphydryl radical is common for all aromatic thioeters.[9]

The mass spectra of **1–9** are also show the odd-electron fragment ions **d**, which are obtained by succesive or simultaneous eliminations of ·X and ·SH radicals and the peaks of the even-electron fragment ions [M-·Br] (ions **e**). In the mass spectra of **4–6**, the even-electron fragment ions [M-·X] (ions **c**) and [M-·Br] (ions **e**) have different structures, but the same values of m/z. Thus, ions **c** and **e** in the case of **4–6** have the same values of percentage of the relative intensity (Table V).

According to literature, the elimination of ·Br radicals is characteristic of the first and second steps of decomposition of molecular ions of 4-ethoxycarbonylalkylthio-5-bromo-6-methyluracils.[10] These processes are not observed for the mass fragmentation of the molecular ions of 2-ethoxycarbonylalkylthio-5-bromo-6-methyluracils[10] and 2,4-dialkoxy-5-bromouracils.[11]



SCHEME 2

Table VII presents for all the compounds investigated **1–9**, the ratios of the intensities of the **b**, **c**, **d**, and **j** ion peaks to those of the parent ion peaks, that is:

μ_1 = int. $[M\text{-}^{\cdot}SH]^+$ / int. $M^{+\cdot}$
μ_2 = int. $[M\text{-}^{\cdot}X]^+$ / int. $M^{+\cdot}$
μ_3 = int. $[M\text{-}^{\cdot}SH\text{-}^{\cdot}X]^{+\cdot}$ / int. $M^{+\cdot}$
μ_4 = int. $[C_7H_6X]^+$ / int. $M^{+\cdot}$

As can be seen from the data in Table VII, the differences between the relative intensities of the peaks of the selected fragment ions **b**, **c**, **d**, **j**, and $M^{+\cdot}$ ions (i.e. the values of μ_1–μ_4 for 2-*ortho*-(*meta*- and *para*-) chloro-(bromo- and nitro-)benzylthio-5-bromo-6-methyluracils **1–9**) are sufficient to differentiate the isomers.

The *ortho*-(*meta*- and *para*-)chloro-(bromo- and nitro-)benzylthio-5-bromo-6-methyluracils **1–9** can be differentiated on the basis of the following sequences of the values of μ_4:

μ_4 *ortho* > μ_4 *para* > μ_4 *meta* **1–3**
μ_4 *para* > μ_4 *ortho* > μ_4 *meta* **4–6**
μ_4 *ortho* > μ_4 *meta* > μ_4 *para* **7–9**

TABLE V Elemental Compositions and Relative Intensities of the Ion Peaks in the Spectra of **1–6** According to High Resolution Data

Ion	m/z	Elemental composition	% Relative intensity					
			1	**2**	**3**	**4**	**5**	**6**
$M^{+\cdot}$								
a	344/346/348	$C_{12}H_{10}N_2OSClBr$	32/43/12	69/94/26	37/50/14			
	388/390/392	$C_{12}H_{10}N_2OSBr_2$				46/88/44	44/97/56	31/56/7
b	311/313/315	$C_{12}H_9N_2OClBr$	6/8/2	41/51/12	19/25/6			
	355/357/359	$C_{12}H_9N_2OBr_2$				1/3/1	17/28/11	8/15/8
c	309/311	$C_{12}H_{10}N_2OSBr$	26/25	3/2	1/1	52/51	7/6	3/2
d	276/278	$C_{12}H_9N_2OBr$	16/15	18/17	9/9	50/49	60/59	19/18
e	265	$C_{12}H_{10}N_2OSCl$	3	3	2			
	309/311	$C_{12}H_{10}N_2OSBr$				52/51	7/6	3/2
f	233/235	$C_6H_6N_2OSBr$	4/4	8/7	2/2	5/4	12/11	3/2
g	220/222	$C_5H_5N_2OSBr$	3/2	3/2	9/8	1/1	3/2	5/4
h	187/189	$C_5H_4N_2OBr$	10/10	4/4	3/2	5/4	13/12	5/4
i	161/163	C_4H_4NOBr	2/2	4/4	4/4	2/1	10/9	11/10
j	169/171	C_7H_6Br				100/99	100/99	100/99
	125	C_7H_6Cl	100	100	100			
k	89	C_7H_5	27	35	16	28	35	17

TABLE VI Elemental Compositions and Relative Intensities of the Ion Peaks in the Spectra of **7–9** According to High Resolution Data

Ion	m/z	Elemental composition	% Relative intensity		
			7	**8**	**9**
$M^{+\cdot}$					
a	355/357	$C_{12}H_{10}N_3O_3SBr$	57/56	100/99	100/99
b	322/324	$C_{12}H_9N_3O_3Br$	4/3	6/5	16/15
c	309/311	$C_{12}H_{10}N_2OSBr$	3/2	14/13	5/4
d	276/278	$C_{12}H_9N_2OBr$	10/9	11/10	21/20
e	276	$C_{12}H_{10}N_3O_3S$	80	60	20
f	233/235	$C_6H_6N_2OSBr$	6/5	9/8	10/9
g	220/222	$C_5H_5N_2OSBr$	24/23	2/1	6/6
h	187/189	$C_5H_4N_2OBr$	18/17	30/29	27/26
i	161/163	C_4H_4NOBr	45/44	8/7	6/3
j	136	$C_7H_6NO_2$	100	51	10
k	89	C_7H_5	25	47	14

The highest values of μ_2 are useful for the differentiation of *ortho*-chloro-(bromo- and nitro-) substituted isomers in the series of **1–3**, **4–6**, and **7–9**. The lowest values of μ_1 are useful for the differentiation of *ortho*-chloro-(bromo)substituted isomers in the series **1–3** and **4–6**.

The *ortho*-(*meta*- and *para*-) substituted isomers of 2-nitrobenzylthio-5-bromo-6-methyluracils (**7–9**) can be distinquished according to the following sequences of the values of μ_1 and μ_3:

μ_1 *para* > μ_1 *ortho*, *meta*
μ_3 *meta* > μ_2 *ortho*, *para*

TABLE VII Values of μ_1–μ_4 Calculated from the EI Mass Spectra of **1–9**

Compound	μ_1	μ_2	μ_3	μ_4
1	0.18	0.60	0.37	2.32
2	0.54	0.03	0.19	1.06
3	0.50	0.02	0.18	2.00
4	0.03	0.59	0.56	1.13
5	0.28	0.07	0.61	1.03
6	0.26	0.05	0.33	1.78
7	0.07	1.07	0.23	1.75
8	0.06	0.01	0.11	0.51
9	0.16	0.05	0.20	0.10

EXPERIMENTAL

The purity of all described compounds was checked by m.p.s, TLC and elemental analysis. Melting points (uncorrected) were determined on a Böetius microscope hot stage. R_f values refer to TLC silica gel F_{254} TLC plates (Merck) developed with $CHCl_3$—MeOH 5:1 and observed under UV light ($\lambda = 254$ and 366 nm). UV/VIS spectra were recorded with a Specord UV/VIS spectrophotometer in methanol. IR spectra were recorded with a FT-IR Bruker IFS-113 v spectrophotometer in KBr pellets. The ^{1}H NMR and ^{13}C NMR spectra were determined with a Varian Gemini 300 (300 MHz) spectrometer in DMSO-d_6 or CD_3OD solution with TMS as internal standard. The ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Varian Gemini 300 spectrometer in DMSO-d_6 or CD_3OD solution at a concentration between 0.25 and 0.40 M in 5 mm sample tubes at ambient temperature. Chemical shifts are given in the δ scale (ppm) and coupling constants in hertz. ^{1}H NMR (300.070) spectra were recorded with spectral width 9 KHz, acquisition time 2.0 s, pulse width 6 μs and double precision acquisition. ^{13}C NMR (75.460 MHz) spectra were recorded with spectral width 18.76 KHz, acquisition time 1.0 s, recycle delay 1.0 s and pulse width 15 μs. Homonuclear ^{1}H-^{1}H shift-correlated two-dimensional diagrams were obtained on a Varian Gemini 300 spectrometer using the COSY pulse sequence. The spectral width was 4.97 KHz, acquisition time 0.206 s, number of increments in t_1 512 and number of scans 16. Heteronuclear 2D ^{13}C NMR- ^{1}H NMR chemical shift correlation experiments were carried out using HETCOR spectra. The spectra were acquired with 2K data points, 256 increments and spectral width 19.63 KHz for ^{13}C and 4.97 KHz for ^{1}H.

Elemental analyses were performed with a Vector Euro EA 3000 analyzer. Low- and high-resolution mass spectra were recorded on an AMD-Intectra GmbH-Harpstedt D-27243 Model 402 two-sector mass spectrometer (ionizing voltage 70 eV, accelerating voltage 8 kV, resolution 10.000). Samples were introduced by a direct insertion probe at the source temperature of $\sim$150°C. The elemental compositions of the ions were determined by a peak matching method relative to perfluorokerosene and using the same instrument. All masses measured were in agreement with those of the composition given in column three of Tables III and IV, to within $\pm$2 ppm. The B/E linked scan spectra in the first field-free region were investigated using helium as the collision gas at a pressure of 1.73×10^{-5} with the ion source temperature of 180°C, ionization energy of 70 eV and an accelerating voltage of 8 kV. The values of μ_1–μ_4, were calculated as averages of three measurements. 2-*ortho*-(*meta*- and *para*-)chloro-(bromo- and

nitro-)benzylthio-6-methyluracil have been obtained according to literature.[4,6]

The Synthesis of 2-*ortho*-(*meta*- and *para*-) chloro-(bromo-and nitro-)benzylthio-5-bromo-6-methyluracils 1–9

A solution of bromine (1 mmol) in 20 ml of carbon tetrachloride was added dropwise during 30 min at room temperature to a stirred suspension of appropriate 2-*ortho*-(*meta*- and *para*-)chloro-(bromo- and nitro-)benzylthio-6-methyluracil (0.5 mmol) in 30 ml of carbon tetrachloride. The reaction mixture was next stirred at room temperature for 2 h. The obtained crude solid product was filtered off, washed with 5 ml of carbon tetrachloride, and dried. The resulting powder was boiled in 10 ml of ethanol under reflux condenser for 5 min. Upon cooling, a solid crystallized from this solution. It was filtered off, washed with 10 ml of cold ethanol, and dried. Compound **1–9** were shown to be analyticaly pure without any further purification (Table I).

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