9-ISOTHIOCYANATOANTHRACENE AS A VERSATILE STARTING COMPOUND IN THE CHEMISTRY OF ANTHRACEN-9-YL DERIVATIVES

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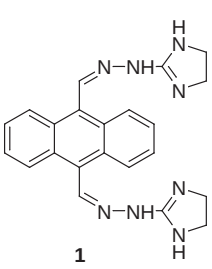
The synthesis, structure and reactivity of 9-isothiocyanatoanthracene (**5**) likewise the conformation of the corresponding thioureas (**6a**–**6i**) have been studied. The ^{13}C NMR substituent chemical shift values of the NCS group and correlations between spectral parameters (IR, NMR) and rate constans of reactions of **5**, acridin-9-yl (**14**), phenyl (**15**) and benzoyl isothiocyanate (**16**) with butylamine were found. Significant increase of the fluorescence of the synthesized anthracenylthioureas with amino acid rests refers to the possibility to use **5** as potential biomarker.

Keywords: Isothiocyanates; Thioureas; 9-Isothiocyanatoanthracene; Anthracenylthioureas; Kinetics; IR spectroscopy; ^{13}C NMR spectroscopy; Fluorescence.

The high chemical reactivity of the NCS group[1] in addition and cyclization reactions made chemists look for various types of isothiocyanates as suitable starting compounds in the synthesis of organic derivatives possessing characteristic biological and physicochemical properties. Interesting results obtained in our previous studies regarding the synthesis and reactivity of acridin-9-yl derivatives[2] prompted us to prepare analogous anthracene compounds. In recent years a variety of anthracene derivatives has received attention as potential antitumor drugs[3], *e.g.* bisantren (9,10-bis substituted anthracene) (**1**). These compounds are typical DNA-intercalating agents where the inhibition of DNA synthesis[4] is based on the ability of the planar anthracene skeleton to incorporate into the stacked base-pairs of DNA double helix. Even some monosubstituted anthracenes as amide derivatives **2** are active against tumor cells[5]. Anthracenones such as anthralin (**3**) are

among the major topical remedies for the treatment of psoriasis[6]. Another anthracene derivatives **4** are well-known as suitable fluorescent reagents for labeling of biomolecules[7]. In order to obtain new fluorogens and biologically interesting compounds, we looked for a convenient starting compound to synthesize a great variety of anthracene derivatives. The long-time experience in the chemistry of isothiocyanates[1] inspired us to choose 9-isothiocyanatoanthracene (**5**) for this purpose.



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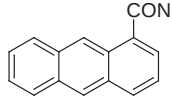

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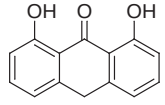

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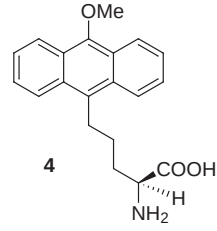

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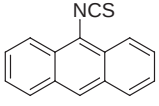
Despite the fact that compound **5** was synthesized already in 1966 (ref.[8]), no data are known regarding its use in organic synthesis in the literature up to now. The aim of this work was to improve the synthesis of **5** and obtain new information on its physicochemical properties, as well as, to study the fluorescence and configuration of synthesized thiourea derivatives as model fluorescent compounds and precursors of new polycyclic systems.

In the meantime, we have found an unexpected regioselectivity in the reaction of 1-(antracen-9-yl)-3-alkylthioureas **6** with bromoacetic acid derivatives to give 2-(anthracen-9-ylimino)-3-alkyl-1,3-thiazolidin-4-ones **7** and 3-(anthracen-9-yl)-2-alkylimino-1,3-thiazolidin-4-ones **8** (refs[9,10]).



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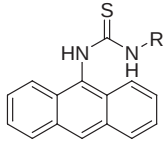

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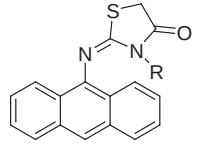

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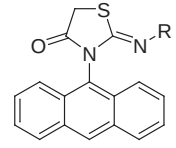

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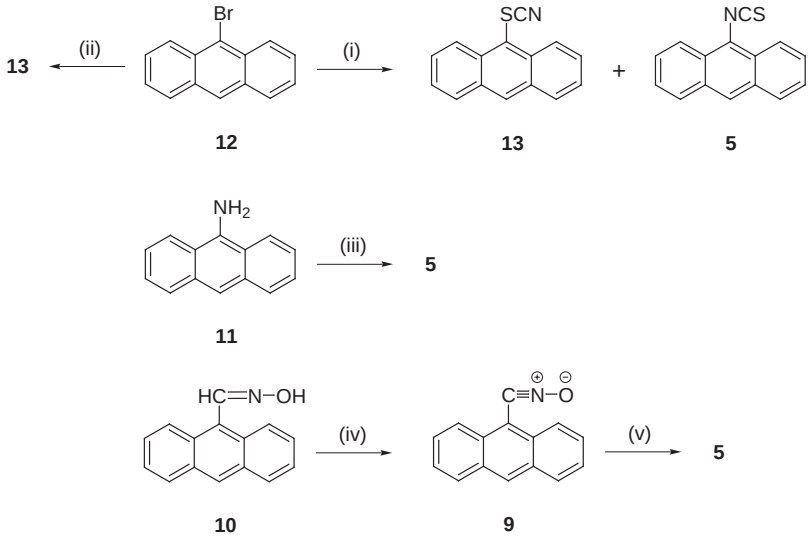
RESULTS AND DISCUSSION

The previously described synthesis of 9-isothiocyanatoanthracene (**5**) was carried out by 1,3-dipolar cycloaddition of anthracene-9-carbonitrile *N*-oxide (**9**), prepared from anthracene-9-carbaldehyde oxime (**10**) and carbon

disulfide in a pressure vessel at 90 °C (ref.[8]). In order to simplify it, we have thoroughly tested other methods, based on 9-aminoanthracene (**11**) and 9-bromoanthracene (**12**), which are usually used for the synthesis of aromatic isothiocyanates[1] (Scheme 1).



(i) AgSCN, I_2, heptane; (ii) KSCN, I_2, heptane; (iii) $CSCl_2$, CH_2Cl_2–H_2O, $NaHCO_3$; (iv) NaOH, NaBrO, H_2O–CH_3CN; (v) KSCN, CH_3OH, $CHCl_3$

SCHEME 1

We found out that 9-bromoanthracene (**12**) reacted neither with silver thiocyanate in toluene at reflux nor with potassium thiocyanate in a mixture dichloromethane–water. The reaction of 9-bromoanthracene (**12**) with silver thiocyanate in heptane in the presence of iodine (i) afforded only 15% of 9-isothiocyanatoantracene (**5**) together with the major product, 9-thiocyanatoanthracene (**13**). The reaction with potassium thiocyanate under the same conditions (ii) yielded only thiocyanate **13**, whereas 9-aminoanthracene (**11**) and thiophosgene yielded (iii) merely 7% of isothiocyanate **5**. However, we succeeded in modifying the anthracene-9-carbonitrile *N*-oxide method[11] by using potassium thiocyanate ((iv), (v)) instead of carbon disulfide, which obviated the need to use pressure and improved the yield of **5** (90%).

To disclose the structure and polarity of the NCS group in **5**, we studied its IR and ^{13}C NMR spectra and kinetics in relation to 9-isothiocyanatoacridine (**14**), phenyl isothiocyanate (**15**) and benzoyl isothiocyanate (**16**)

(Table I). The results of kinetic measurements of Ad_N reactions of isothiocyanates **5**, **14**, **15** and **16** with butylamine (log *k*) allowed to estimate the range of reactivity of the NCS group, which decreased in the order benzoyl > acridin-9-yl > anthracen-9-yl > phenyl (Table I).

We were also interested in the relation between the reactivity and spectral characteristics. From comparison of ^{13}C chemical shifts of the NCS group (Table I) follows that the NCS carbon in **14** is strongly deshielded (140.8 ppm) due to the electron-acceptor effect of the heterocyclic nitrogen, though not so much as under the influence of the carbonyl group in **16** (147.6 ppm). In contrast, chemical shifts of the NCS carbon in **5** (137.5 ppm) and **15** (135.2 ppm) reflect a weaker deshielding by the anthracene or benzene ring. Linear relationships between spectral characteristics of the electrophilic NCS carbon and the reactivity of the NCS group derived from Table I (log k – ν_{as}(NCS), correlation coefficient r = 0.995; log k – δ^{13}C(NCS), r = 0.989; log k – δ^{13}C(C-NCS), r = 0.921) confirmed the dominance of polar effects in the studied compounds.

As it is known, the NCS group interacts with the benzene ring by the +M and –I effect[1]. The substituent-induced chemical shifts (SCS) of the NCS group in **5**, **14** and **15** are shown and compared one with another in Table II.

The NCS group bound to the anthracen-9-yl or acridin-9-yl group, in accord with its pseudohalogen character, shields the *ipso* carbon and carbons C-8a,9a, resembling bromo and not amino substituent. Marked shielding of

TABLE I
Spectral characteristics of isothiocyanates **5**, **14**, **15**, **16** and the rate constants of their reaction with butylamine in acetonitrile at 25 °C

Compound	ν_{as}(NCS), cm^{-1}	^{13}C NMR(NCS) ppm	^{13}C NMR(C–NCS) ppm	log k k, l mol^{-1} s^{-1}
5	2 095	137.46	131.40	–0.374 0.423
14	2 060[a]	140.80[a]	132.50[a]	1.230 16.97[b]
15	2 110	135.24[c]	130.94[c]	–0.512 0.304
16	1 896[d]	147.60[c]	161.60[c]	3.461 2 893[f]

[a] Ref.[12]; [b] ref.[13]; [c] ref.[14]; [d] ref.[15]; [e] ref.[16]; [f] ref.[17]

carbons C-1,8 is also observed, whereas carbons C-3 to C-6, C-4a,10a and C-10 are practically insensitive to the substituent effect.

Starting from compound **5**, 1-(anthracen-9-yl)-3-substituted thioureas **6a**–**6l**, as fluorescent model compounds and intermediates for heterocycles[9], have been prepared by addition of primary and secondary amines and L-amino acids to **5** in dichloromethane (Scheme 2).

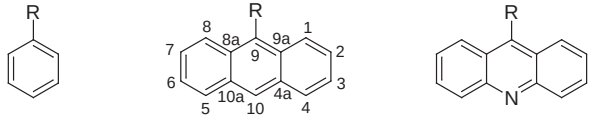
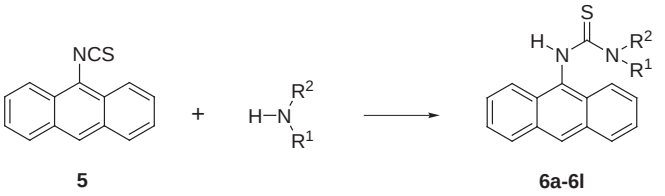


TABLE II
The ^{13}C NMR substituent chemical shift values of compound **5**, **14**, **15** and related derivatives

Compound	R	SCS[a]								Ref.
		C-1,8	C-2,7	C-3,6	C-4,5	C-9 *ipso*	C-8a,9a *ortho*	C-4a,10a *meta*	C-10 *para*	
Phenyl	NCS					2.8	–2.8	1.0	–1.2	18[b]
	NH_2					19.2	–12.4	1.3	–9.5	19[b]
	Cl					6.4	0.2	1.0	–2.0	19[b]
	Br					–5.4	3.3	2.2	–1.0	19[b]
9-Anthryl	NCS	–5.1	2.0	0.8	0.7	–4.0	–4.0	–0.4	0.3	
	NH_2	–7.1	–1.6	–0.2	0.8	11.7	–13.4	0.5	–9.9	20[b]
	Cl	–3.4	1.4	0.3	0.3	1.9	–2.8	0.2	–0.2	20[b]
	Br	–0.5	1.8	0.3	0.4	–3.9	–1.1	0.5	0.9	20[b]
Acridin-9-yl	NCS	–7.8	1.1	2.0	0.1	–3.7	–5.0	–0.4		21[b]
	NH_2	–6.8	–2.3	–0.4	–0.2	14.4	–12.9	0.5		22[c]
	Cl	–6.0	1.0	1.8	0.1	4.8	–2.5	–0.4		21[b]
	Br	–0.5	1.1	0.4	0.7	–5.2	–0.7	–0.2		22[c]

[a] SCS (in ppm) = ^{13}C chemical shifts of respective carbons of R-substituted compounds minus ^{13}C chemical shifts of the compound with R = H. [b] Solvent $CDCl_3$. [c] Solvent DMSO-d_6.



5 **6a-6l**

6	**a**	**b**	**c**	**d**	**e**	**f**	**g**	**h**	**i**
R^1	H	H	H	H	H	H	methyl	ethyl	propyl
R^2	ethyl	propyl	butyl	*tert*-butyl	*sec*-butyl	furfuryl	cyclohexyl	ethyl	propyl

	j	**k**	**l**
HNR^1R^2	Gly	Ala	Phe

SCHEME 2

The reaction of **5** with aniline in dichloromethane did not provide the expected thiourea. The same reaction under reflux in acetonitrile, which enhanced an analogous reaction of phenyl isothiocyanate with aniline approximately six times compared with dichloromethane[23], afforded only a low yield of the corresponding thiourea.

It is known that 1-arylthioureas **17a** and 1-aryl-3-alkylthioureas **17b** adopt *E* conformation on the (aryl–)N–C(=S) bond[24,25]. The reason is the stabilization of the *E* isomer only by intramolecular interaction of the N′H proton with a π-orbital of the aromatic ring (Fig. 1).

We have studied the conformation of 1-(anthracen-9-yl)-3-alkyl-substituted thioureas **6a**–**6f** by IR spectroscopy in tetrachloromethane using a Magna System 750 spectrophotometer and confirmed the same *E*

E *E*

17a **17b**

IR (CCl_4): ν(NH) = 3 420, $\nu_{as}(N'H_2)$ = 3 521, $\nu_s(N'H_2)$ = 3 398
R = *sec*-butyl: ν(NH) = 3 419, ν(N′H) = 3 389
R = *tert*-butyl: ν(NH) = 3 415, ν(N′H) = 3 388

FIG. 1
Stabilization of *E* conformation in compounds **17a, 17b** and its influence on IR spectra

conformation. Similarly to 1-phenyl-3-alkylthioureas[25], the ν(NH) band at a higher wavelength (3 402–3 404 cm^{-1}), whose position is insensitive to the change of the 3-substituent, can be attributed to the anthracene N–H bond whereas the absorption band at 3 373–3 394 cm^{-1} to the alkyl N′–H bond. In three substituted thioureas **6g**–**6i**, stabilization by the hydrogen bond cannot occur. Therefore, two absorption bands observed for these compounds, one above 3 400 cm^{-1} assigned in accord with ref.[25] to the *E* isomer and the other below 3 400 cm^{-1} assigned to the *Z* isomer, evidence that both possible isomers are present. An approximate ratio of isomers can be assessed from the intensity of respective bands: in **6i**, the intensity of both bands is equal, **6g** shows the more intensive absorption band of the *Z* isomer at 3 373 cm^{-1} and **6h** of the *E* isomer at 3 417 cm^{-1} (Fig. 2).

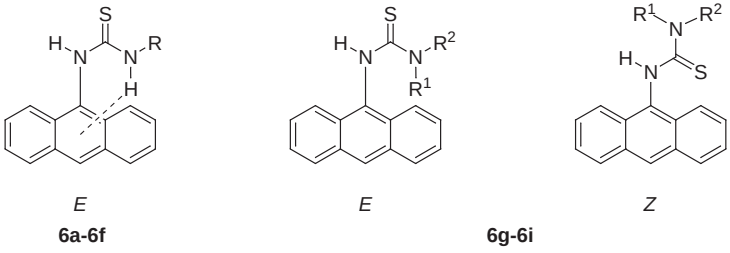


FIG. 2
Conformations of thioureas **6a**–**6i**

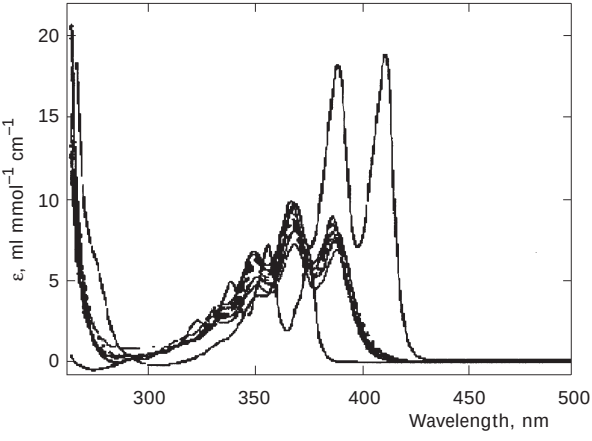


FIG. 3
UV-VIS spectra of anthracene, 9-isothiocyanatoanthracene (**5**) and 1-alkyl-(3-anthracene-9-yl)-thioureas **6a**–**6h**

Four typical intensive UV bands of **6a**–**6i** show a hypsochromic shift of λ_{max} in comparison with **5** (Fig. 3, Table III). Figure 4 depicts fluorescence spectra of compounds **5**, **6a**–**6h** and anthracene.

Each of the synthesized compounds **6a**–**6l** except of the thioureas with *sec*-aminorests **6g**–**6i** are characterized by enhanced intensity of fluorescence according to the standard **5**. The highest fluorescence has been observed in the case of the aminoacid derivatives **6j**–**6l** (F/F_0 = 35.29–57.11;

TABLE III
UV-VIS and fluorescence properties of anthracene and its derivatives **5**, **6a**–**6h**, **6j**–**6l**

Comp.	Absorbance λ_{max}, nm ε, ml mmol^{-1}cm^{-1}	$\varepsilon_{385\ nm}$ ε, ml mol^{-1} cm^{-1}	Fluorescence λ_{max}, nm *F*, a.u. (F/F_0)	Sensitivity $F_{max} \times \varepsilon_{385\ nm}$	Efficiency $F_{max}/\varepsilon_{385\ nm}$
6a	366.0 9.93	9.02	435.6 12.7 (7.3)	114.55	1.40
6b	365.8 8.84	8.03	434.4 10.4 (6.0)	83.51	1.29
6c	366.0 9.34	8.49	436.0 10.0 (5.7)	84.90	1.17
6d	366.0 8.49	7.70	434.8 7.34 (4.2)	56.51	0.95
6e	367.4 8.73	7.87	439.4 3.11 (1.8)	24.48	0.39
6f	366.0 9.89	8.88	433.6 9.81 (5.6)	87.11	1.10
6g	367.9 8.13	7.29	No fluorescence	–	–
6h	367.8 7.26	6.48	No fluorescence	–	–
6j	365.2 9.08	7.94	428.0 64.0 (37.64)	508.16	8.06
6k	365.2 7.73	6.83	432.0 60.0 (35.29)	409.80	8.78
6l	365.4 10.29	8.93	428.0 87.0 (51.17)	776.91	9.74
5	410.2 18.89	16.25	443.0 1.7 (1.0)	27.63	0.105
Anthracene	355.4 7.27	6.69[a]	426.0 440.2 (253.0)	2 944.9[b]	65.80[c]

[a] $\varepsilon_{374\ nm}$; [b] $F_{max} \times \varepsilon_{374\ nm}$; [c] $F_{max}/\varepsilon_{374\ nm}$.

Table III). No general conclusions on the relation between the structure and fluorescence of the prepared compounds could be made.

Preliminary fluorescence studies with amino acid derivatives **6j**–**6l** show potential use of 9-isothiocyanatoanthracene (**5**) as fluorescence marker for peptides and proteins. Further studies in this directions are under way.

EXPERIMENTAL

Melting points were determined on a Koffler hot-stage apparatus and are uncorrected. Elemental analysis was done on a Perkin–Elmer analyzer CHN 2400. The reaction course and purity of products were followed by thin-layer chromatography on Silufol plates (Kavalier). Spots were detected by UV light at λ = 254 nm. Preparative column chromatography was done on a Kieselgel Merck 60, type 9385 or 100, the grain size 250 μm. IR spectra (cm^{-1}) were recorded on a Specord 75 IR spectrophotometer (Zeiss) in chloroform and on a Magna System 750 spectrophotometer in tetrachloromethane or in KBr tablets. UV spectra (λ, nm; ε, ml $mmol^{-1}$ cm^{-1}) were obtained using a Specord M42 spectrophotometer (Zeiss; concentration $5 \cdot 10^{-5}$ mol l^{-1}) and a Shimadzu UV spectrophotometer ($1 \cdot 10^{-6}$ mol l^{-1} in acetonitrile). Fluorescence measurements (nm) were performed on a Shimadzu RF-5000 spectrophotometer in acetonitrile ($1 \cdot 10^{-6}$ mol l^{-1}). Emission spectra were recorded in the 420–550 nm region at the excitation wavelength 385 nm. Fluorescence parameters are the averages of 3–6 subsequent scans at the same excitation wavelength. Fluorescence intensities measured at room temperature are expressed in arbitrary units (a.u.). ^{1}H NMR spectra were measured on a Tesla BS 587A spectrometer (80 MHz) and ^{13}C NMR spectra on a Varian Gemini 2000 NMR spectrometer (75 MHz) at room temperature. Chemical shifts are given in

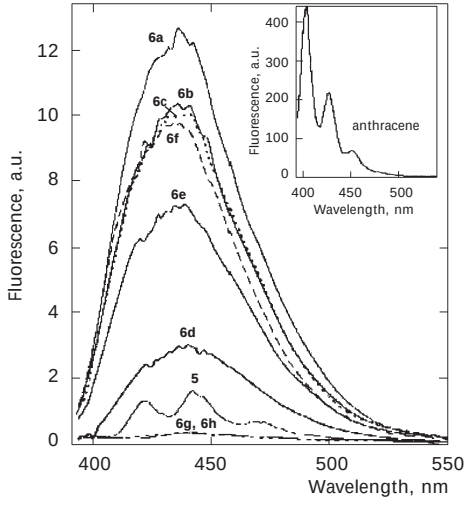


FIG. 4
Fluorescence of anthracene, 9-isothiocyanatoanthracene (**5**) and 1-alkyl-(3-anthracene-9-yl)-thioureas **6a**–**6h**

ppm (δ-scale), coupling constants (*J*) in Hz. Samples **6j**–**6l** were dissolved in deuterioacetone and **5**, **6a**–**6i** in deuteriochloroform with TMS added as an internal standard.

Kinetic Measurements

Kinetics of reactions of 9-isothiocyanatoanthracene and phenyl isothiocyanate with butylamine was followed by UV spectroscopy on a Specord M42 spectrophotometer at 25 °C in acetonitrile. Concentration of isothiocyanates ($5 \cdot 10^{-5}$ mol l^{-1}) and that of amine ($5 \cdot 10^{-3}$ mol l^{-1}) ensured the pseudo first-order reaction. The apparent rate constants k' (s^{-1}) were determined from the slope of the linear relationship log [log (A_∞/A_t)] *vs* time *t*. The values of rate constant *k* (l mol^{-1} s^{-1}) were obtained by dividing the k' values by concentration of amine.

Chemicals

Anthracene-9-carbaldehyde, 9-bromoanthracene, 9-nitroanthracene, amines and hydroxylamine hydrochloride were commercial products (Aldrich), purified by crystallization. Acetonitrile (Avocado) was dried over phosphorus pentoxide and distilled. All the L-amino acids used were commercial products (Sigma).

(*Z*)-Anthracene-9-carbaldehyde Oxime (**10**)

The procedure described in refs[26,27] was modified as follows: To a solution of the aldehyde (300 mg, 1.45 mmol) in ethanol (7 ml), a solution of hydroxylamine hydrochloride (101 mg, 1.45 mmol) in a small volume of water neutralized with sodium carbonate (80 mg, 0.75 mmol) was added. The mixture was refluxed for 15 min, filtered with charcoal, the oxime deposited on standing was filtered off and dried. Yield 95%, m.p. 165–166 °C.

Anthracene-9-carbonitrile *N*-Oxide (**9**)

The procedure described in ref.[11] was modified as follows: To a solution of sodium hydroxide (0.56 g, 14 mmol) in water (15 ml) (*Z*)-anthracene-9-carbaldehyde oxime (**10**) (1 g, 4.52 mmol) in acetonitrile (15 ml) was added. This solution was added dropwise at 0 °C to a water solution (25 ml) of sodium hypobromite prepared from sodium hydroxide (0.39 g, 9.75 mmol) and bromine (0.115 g, 0.725 mmol). The mixture was stirred for 15 min, the precipitate of **9** was filtered off and dried. Yield 90%, m.p. 128–129 °C.

9-Isothiocyanatoanthracene (**5**)

The procedure used for preparation of 2,4,6-trimethylphenyl isothiocyanate[28] was modified as follows: To a solution of **9** (1 g, 4.5 mmol) in chloroform (10 ml), a solution of potassium thiocyanate (0.43 g, 4.5 mmol) in methanol (20 ml) was added and the product **5** deposited. Solvents were evaporated under diminished pressure and the product was purified by column chromatography on silicagel (cyclohexane as a mobile phase). Yield 80%, m.p. 138–139 °C. For $C_{15}H_9NS$ (235.3) calculated: 76.56% C, 3.58% H, 5.95% N; found: 76.40% C, 3.92% H, 5.94% N. IR: 3 094, 3 064, 3 015 (C-H); 2095 (NCS); 1 618, 1 580 (C=C). ^{1}H NMR: 8.35 s, 1 H (H-10); 7.38–8.32 m, 8 H (anthracene). ^{13}C NMR: 137.46 (NCS), 123.01 (C-1, C-8), 127.32 (C-2, C-7), 126.12 (C-3, C-6), 128.75 (C-4, C-5), 131.40 (C-4a, C-10a), 127.82

(C-8a, C-9a), 122.16 (C-9), 126.45 (C-10). UV (acetonitrile): 368.8 (3.21), 388.8 (3.41), 410.2 (3.40).

9-Aminoanthracene (**11**) was prepared by reduction of 9-nitroanthracene with tin dichloride in acetic acid and hydrochloric acid according to ref.[29]. 1-Butyl-3-phenylthiourea was prepared from phenyl isothiocyanate and butylamine in ethanol[30] and a standard sample of 9-thiocyanatoanthracene (**13**) according to ref.[31].

Preparation of 1-Alkyl-3-(anthracen-9-yl)thioureas **6a**–**6i**.
General Method

To a solution of **5** (100 mg, 0.425 mmol) in dichloromethane (5 ml), an equimolar amount of corresponding amine was added. After the end of reaction (TLC), dichloromethane was distilled off at reduced pressure and thiourea was crystallized from dichloromethane–heptane.

1-(Anthracen-9-yl)-3-ethylthiourea (**6a**): Yield 86%, m.p. 195–196 °C. For $C_{17}H_{16}N_2S$ (280.4) calculated: 72.82% C, 5.75% H, 9.99% N; found: 72.54% C, 5.63% H, 9.62% N. IR ($CHCl_3$): 3 395 (NH); 1 606 (C=C); 1 525, 1 477, 1 100 (NHCS). IR (CCl_4): 3 404 $\nu_{(E)}$(NH), 3 390 $\nu_{(Z)}$(NH). ^{1}H NMR: 8.50 s, 1 H (H-10); 7.38–8.31 m, 8 H (anthracenyl); 5.33 bs, 1 H (NH); 3.50 q, 2 H, J = 6.1 (CH_2); 0.93 t, 3 H, J = 6.1 (CH_3). ^{13}C NMR: 181.80 (C=S); 128.82, 127.70, 126.13, 122.91 (C-1 to C-8); 131.87 (C-4a, 10a); 129.17 (C-8a, 9a); 127.10 (C-9); 128.59 (C-10); 40.39 (CH_2); 14.37 (CH_3).

1-(Anthracen-9-yl)-3-propylthiourea (**6b**): Yield 84%, m.p. 185–187 °C. For $C_{18}H_{18}N_2S$ (294.4) calculated: 73.44% C, 6.16% H, 9.51% N; found: 73.17% C, 6.26% H, 9.72% N. IR ($CHCl_3$): 3 395 (NH); 1 622, 1602 (C=C); 1 520, 1 345, 1 100 (NHCS). IR (CCl_4): 3 404 $\nu_{(E)}$(NH), 3 394 $\nu_{(Z)}$(NH). ^{1}H NMR: 8.54 s, 1 H (H-10); 7.38–8.34 m, 8 H (anthracenyl); 5.38 bs, 1 H (NH); 3.25–3.75 m, 2 H (N-CH_2); 1.38 m, 2 H (CH_2); 0.93 t, 3 H, J = 7.4 (CH_3).

1-(Anthracen-9-yl)-3-butylthiourea (**6c**): Yield 68%, m.p. 181–183 °C. For $C_{19}H_{20}N_2S$ (308.5) calculated: 73.99% C, 6.54% H, 9.08% N; found: 74.01% C, 6.61% H, 9.23% N. IR ($CHCl_3$): 3 405 (NH); 1 622, 1 588 (C=C); 1 522, 1 347, 1 100 (NHCS). IR (CCl_4): 3 404 $\nu_{(E)}$(NH), 3 392 $\nu_{(Z)}$(NH). ^{1}H NMR: 8.47 s, 1 H (H-10); 7.25–8.33 m, 8 H (anthracenyl); 5.33 bs, 1 H (NH); 3.25–3.68 m, 2 H (N-CH_2); 0.50–1.50 m, 7 H ($CH_3CH_2CH_2$). MS (*m/z*, % rel. int.): 308 (24) [$M^{\bullet+}$], 251 (23) [$M^{\bullet+} - C_4H_9$], 235 (47) [$M^{\bullet+} - C_4H_9NH_2$], 210 (35), 192 (100) [$C_{14}H_{10}N$], 165 (45).

1-(Anthracen-9-yl)-3-tert-butylthiourea (**6d**): Yield 67%, m.p. 195–197 °C. For $C_{19}H_{20}N_2S$ (308.5) calculated: 73.99% C, 6.54% H, 9.08% N; found: 74.22% C, 6.31% H, 9.35% N. IR ($CHCl_3$): 3 370 (NH); 1 630 (C=C); 1 535, 1 510, 1 132 (NHCS). IR (CCl_4): 3 404 $\nu_{(E)}$(NH), 3 375 $\nu_{(Z)}$(NH). ^{1}H NMR: 8.51 s, 1 H (H-10); 7.38–8.17 m, 8 H (anthracenyl); 5.33 bs, 1 H (NH); 1.30 s, 9 H (3 × CH_3).

1-(Anthracen-9-yl)-3-sec-butylthiourea (**6e**): Yield 62%, m.p. 186–187 °C. For $C_{19}H_{20}N_2S$ (308.5) calculated: 73.99% C, 6.54% H, 9.08% N; found: 73.70% C, 6.31% H, 9.30% N. IR ($CHCl_3$): 3 405, 3 375 (NH); 1 625, 1 602 (C=C); 1 510, 1 475, 1 155 (NHCS). IR (CCl_4): 3 402 $\nu_{(E)}$(NH), 3 373 $\nu_{(Z)}$(NH). ^{1}H NMR: 8.51 s, 1 H (H-10); 7.32–8.35 m, 8 H (anthracenyl); 5.00 bs, 1 H (NH); 4.12–4.62 m, 1 H (CH); 1.00–1.47 m, 2 H (CH_2); 0.96 d, 3 H, J = 6.8 (CH_3); 0.70 t, J = 7.3 (CH_3).

1-(Anthracen-9-yl)-3-furfurythiourea (**6f**): Yield 71%, m.p. 183–185 °C. For $C_{20}H_{16}N_2OS$ (332.4) calculated: 72.26% C, 4.85% H, 8.43% N; found: 72.01% C, 4.93% H, 8.52% N. IR ($CHCl_3$): 3 392 (NH); 1 605 (C=C); 1 530, 1 475, 1 110 (NHCS). IR (CCl_4): 3 402 $\nu_{(E)}$(NH),

3 392 $\nu_{(Z)}$(NH). ^{1}H NMR: 8.54 s, 1 H (H-10); 7.35–8.30 m, 8 H (anthracenyl); 7.13 bs, 1 H (H-5-furfuryl); 5.97–6.30 m, 2 H (H-3-furfuryl, H-4-furfuryl); 5.62 bs, 1 H (NH); 4.76 d, 2 H, *J* = 5.0 (CH_2).

3-(Anthracen-9-yl)-1-cyclohexyl-1-methylthiourea (**6g**): Yield 88%, m.p. 173–175 °C. For $C_{22}H_{24}N_2S$ (348.5) calculated: 75.82% C, 6.94% H, 8.04% N; found: 76.00% C, 7.10% H, 8.21% N. IR ($CHCl_3$): 3 420, 3 380 (NH); 1 625, 1 600 (C=C), 1 490, 1 445, 1 110 (NHCS). IR (CCl_4): 3 413 $\nu_{(E)}$(NH), 3 373 $\nu_{(Z)}$(NH). ^{1}H NMR: 8.38 s, 1 H (H-10); 7.30–8.25 m, 8 H (anthracenyl); 4.98 m, 1 H (CH); 3.01 s, 3 H (CH_3); 0.97–2.10 m, 11 H (cyclohexyl).

3-(Anthracen-9-yl)-1,1-diethylthiourea (**6h**): Yield 87%, m.p. 145–147 °C. For $C_{19}H_{20}N_2S$ (308.5) calculated: 73.99% C, 6.54% H, 9.08% N; found: 74.03% C, 6.63% H, 9.23% N. IR ($CHCl_3$): 3 425 (NH); 1 626, 1 605 (C=C); 1 502, 1 440, 1 142 (NHCS). IR (CCl_4): 3 417 $\nu_{(E)}$(NH), 3 367 $\nu_{(Z)}$(NH). ^{1}H NMR: 8.41 s, 1 H (H-10); 7.30–8.25 m, 8 H (anthracenyl); 7.30 bs, 1 H (NH); 3.90 q, 4 H, *J* = 7.4 (CH_2); 1.39 t, 6 H, *J* = 7.4 (CH_3). ^{13}C NMR: 182.23 (C=S); 128.83, 126.69, 125.43, 123.38 (C-1 to C-8); 131.83 (C-4a, C-10a); 129.50 (C-8a, C-9a); 130.98 (C-9); 127.09 (C-10); 46.01 (CH_2); 13.07 (CH_3).

3-(Anthracen-9-yl)-1,1-dipropylthiourea (**6i**): Yield 85%, m.p. 163–165 °C. For $C_{21}H_{24}N_2S$ (336.5) calculated: 74.96% C, 7.19% H, 8.32% N; found: 75.02% C, 7.31% H, 8.41% N. IR ($CHCl_3$): 3 420 (NH); 1 602 (C=C); 1 500, 1 485, 1 100 (NHCS). IR (CCl_4): 3 404 $\nu_{(E)}$(NH), 3 392 $\nu_{(Z)}$(NH). ^{1}H NMR: 8.46 s, 1 H (H-10); 7.37–8.25 m, 8 H (anthracenyl); 7.32 bs, 1 H (NH); 3.63–3.95 m, 4 H (N-CH_2); 1.60–2.20 m, 4 H (CH_2); 1.00 t, 6 H, *J* = 7.4 (CH_3).

Preparation of 3-(Anthracen-9-yl)thioureido Amino Acids **6j**–**6l**.
General Method

The following modified procedure was used[32]: To a solution of the corresponding amino acid (0.43 mmol) in water (1.11 ml) which had been adjusted to pH 10 with 1 M NaOH, a solution of 9-isothiocyanatoanthracene (**5**) (70 mg, 0.29 mmol) in 1,4-dioxane (3 ml) was added and the mixture was heated to 80 °C untill the end of the reaction (TLC, cyclohexane). The reaction mixture was poured into water (10 ml) and 1 M HCl was added dropwise till a crude product precipitated. Obtained compounds were filtered off, washed with water and crystallized from the mixture acetone–diethylether–heptane .

[3-(Anthracen-9-yl)thioureido]acetic acid (**6j**): Yield 80%, m.p. 111–113 °C. For $C_{17}H_{14}N_2O_2S$ (310.4) calculated: 65.79% C, 4.55% H, 9.03% N; found: 65.83% C, 4.63% H, 9.62% N. IR (KBr): 3 336 (NH); 1 715 (C=O); 1 620 (C=C); 1 530, 1 435, 1 135 (NHCS). ^{1}H NMR: 9.40 bs, 1 H (NH); 8.66 s, 1 H (H-10); 7.38–8.43 m, 8 H (anthracenyl); 6.75 bs, 1 H (NH); 4.24 s, 2 H (CH_2).

(S)-2-[3-(Anthracen-9-yl)thioureido]propanoic acid (**6k**): Yield 72%, m.p. 185–187 °C. For $C_{18}H_{16}N_2O_2S$ (324.4) calculated: 66.65% C, 4.97% H, 8.64% N; found: 66.33% C, 5.03% H, 8.72% N. IR (KBr): 3 362, 3 261 (NH); 1 705 (C=O); 1 618 (C=C); 1 522, 1 435, 1 170 (NHCS). ^{1}H NMR: 9.37 bs, 1 H (NH); 8.65 s, 1 H (H-10); 7.25–8.43 m, 8 H (anthracenyl); 6.58 bs, 1 H (NH); 5.16 m, 1 H (CH); 1.24 d, 3 H (CH_3).

(S)-2-[3-(Anthracen-9-yl)thioureido]-3-phenylpropanoic acid (**6l**): Yield 40%, m.p. 190–193 °C. For $C_{24}H_{20}N_2O_2S$ (400.5) calculated: 71.98% C, 5.03% H, 6.99% N; found: 72.03% C, 5.23% H, 6.82% N. IR (KBr): 3 365, 3 296 (NH); 1 705 (C=O); 1 620 (C=C); 1 517, 1 435, 1 130 (NHCS). ^{1}H NMR: 9.41 bs, 1 H (NH); 8.66 s, 1 H (H-10); 6.50–8.38 m, 8 H (anthracenyl); 6.08 bs, 1 H (NH); 5.40 m, 1 H (CH); 2.92 d, 2 H (CH_2).

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