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SYNTHESIS OF 2-(*N*-BENZOYLIMINO)-*N*-(9,10-DIOXO-9,10-DIHYDROANTHRACEN-1-YL)THIAZOLES

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N-Aroylthioureas hold a significant promise for the synthesis of such heterocycles as imidazolidine-2-thiones [1, 2], 2-aroyliminothiazolines [3-5], 1,2,4-triazoles [6], 1,3-thiazines [7], and indeno[1,2-*d*]-[1,3]thiazepines [8]. Of particular interest are 2-iminothiazolines, which are characterized by a wide range of biological properties [9-11]. For example, the thiazol-2-imine fragment is a structural fragment in muscarinic agonists, as well as antifungal, hypolipidemic, antidiabetic, anti-inflammatory, analgesic, and anti-shistosomiasis compounds [5]. Thiazoline derivatives are also used as insecticides and plant growth regulators [5].

The reaction of *N,N*'-disubstituted thioureas with α-bromo ketones has been described in the literature [5, 12], and it provides access to various *N*-substituted 2-iminothiazoles. However, 2-iminothiazoles with 9,10-dioxo-9,10-dihydroanthracenyl substituents at position 3 of the heterocycle remain hitherto unknown. The pronounced biological properties of anthraquinone derivatives [13-15] motivate the search for hybrid structures that include both anthraquinone and thiazole ring systems.

Based on these considerations, we treated our previously described *N*-benzoyl-*N*'-(9,10-dioxo-9,10-dihydroanthracen-1-yl)thioureas **1a**-**e** [16] with *in situ* generated α-bromoacetone in the presence of triethylamine and obtained the 2-(*N*-benzoylimino)-*N*-(9,10-dioxo-9,10-dihydroanthracen-1-yl)thiazoles **2a**-**e** in 48-68% yields. The formation of 2-(*N*-benzoyl)imine type thiazoles through a cyclocondensation with the participation of aminoanthracene nitrogen atom was in agreement with the recently described reactions of *N*-aryl-*N*'-aroylthioureas with α-halo ketones [4, 12, 13].

The ^{1}H NMR spectra of compounds **2a**-**e** contained thiazole H-5 proton singlets at 6.89-7.01 ppm and methyl group singlets at 1.97-2.04 ppm, besides the CH signals of the aromatic rings. The formation of a thiazole ring was also clearly confirmed by the ^{13}C spectra containing the characteristic C-4 singlets at 106.1-107.2 ppm, C-5 singlets at 139.3-144.9 ppm, and C-2 singlets at 168.2-169.7 ppm. The ^{13}C signals of the thiazole 4-CH_3 substituent were found at 13.7-14.2 ppm, which is typical for 3-aryl-2-benzoylimino-4-methyl-1,3-thiazolines [4, 5].

Thus, we have prepared new 2-(*N*-benzoylimino)-*N*-(9,10-dioxo-9,10-dihydroanthracen-1-yl)thiazoles by a novel route, starting from *N*-benzoyl-*N*'-(9,10-dioxo-9,10-dihydroanthracen-1-yl)thioureas.

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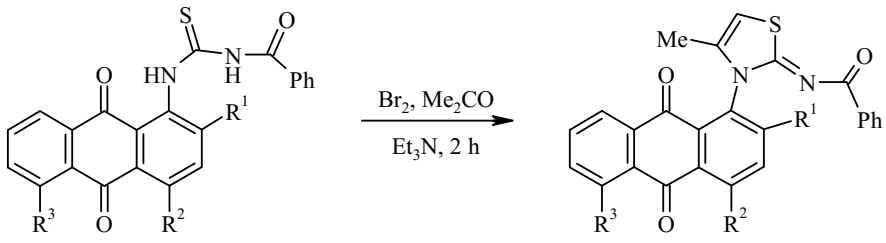

1a–e **2a–e**

a $R^1 = R^2 = R^3 = H$; **b** $R^1 = Me$, $R^2 = R^3 = H$; **c** $R^1 = R^3 = H$, $R^2 = NH_2$;
d $R^1 = R^2 = H$, $R^3 = NH_2$; **e** $R^1 = R^3 = H$, $R^2 = NHCOPh$

IR spectra were recorded on a Specord M80 spectrometer in KBr pellets. ^1H and ^{13}C NMR spectra were acquired on a Varian Mercury 400 instrument (400 and 100 MHz, respectively) at 25°C in DMSO-d_6, with TMS as internal standard. Chromatography with mass spectrometry was performed on an Agilent 1100 Series chromatograph, equipped with an Agilent LC/MSDSL mass selective detector. A Zorbax SB-C18 column (1.8 μ, 4.6×15 mm) was used with a mobile phase gradient from acetonitrile–water–0.1% TFA (system A) to water–0.1% TFA (system B). Chemical ionization was used at ambient pressure. The reaction progress was monitored by TLC on Silufol UV-254 plates with a 6:1 benzene–acetonitrile mobile phase. The elemental analysis was performed on a Thermo Finnigan Flash EA 1112 instrument.

Preparation of *N*-[3-(9,10-Dioxo-9,10-dihydroanthracen-1-yl)-4-methyl-1,3-thiazol-2(3*H*)-ylidene]-benzamides 2a-e (General Method). A solution of bromine (0.0384 ml, 0.749 mmol) in acetone (10 ml) was added with stirring over 15 min to a suspension of *N*-benzoylthiourea **1a-e** (0.749 mmol) and triethylamine (0.104 ml, 0.749 mmol) in acetone (30 ml). The reaction mixture was maintained at the room temperature for 2 h, the precipitate that formed was filtered off, washed with acetone, then with water, dried, and crystallized from toluene.

***N*-[3-(9,10-Dioxo-9,10-dihydroanthracen-1-yl)-4-methyl-1,3-thiazol-2(3*H*)-ylidene]benzamide (2a)**. Yield 68%; mp 210-211°C. IR spectrum, ν, cm^{-1}: 1680, 1631 (C=O quinone), 1685 (C=O amide), 1471 (C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.99 (3H, s, CH_3); 6.92 (1H, s, CH=); 6.94-7.02 (3H, m, H Ar); 7.68-7.70 (3H, m, H Ph); 7.91-8.05 (2H, m, H Ph); 8.15-8.28 (3H, m, H Ar); 8.53 (1H, d, *J* = 8.4, H Ar). ^{13}C NMR spectrum, δ, ppm: 14.2 ($\underline{C}H_3CH$=); 106.7 (CH=); 126.8, 127.3, 127.5, 128.4 (C Ar); 128.7, 129.1, 129.3, (C Ph); 131.5 (C Ar); 132.4 (C Ph); 133.5, 133.6, 134.4, 134.9, 135.2 (C Ar); 135.8 (C Ph); 137.8 (C–N); 143.3 ($CH_3\underline{C}H$=); 168.5 (C=N); 173.5 (COPh); 181.8 (CO); 182.5 (CO). Mass spectrum, *m*/*z* (I_{rel}, %): 425 $[M+H]^+$ (69). Found, %: C 70.64; H 3.87; N 6.71; S 7.59. $C_{25}H_{16}N_2O_3S$. Calculated, %: C 70.74; H 3.80; N 6.60; S 7.55.

***N*-[4-Methyl-3-(2-methyl-9,10-dioxo-9,10-dihydroanthracen-1-yl)-1,3-thiazol-2(3*H*)-ylidene]benzamide (2b)**. Yield 51%; mp 206-207°C. IR spectrum, ν, cm^{-1}: 1681, 1623 (C=O quinone), 1670 (C=O amide), 1397 (C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.99 (3H, s, CH_3); 2.17 (3H, s, CH_3); 7.01 (1H, s, CH=); 7.24-7.27 (2H, m, H Ph); 7.31-7.40 (1H, m, H Ph); 7.67-7.74 (2H, m, H Ph); 7.85-7.90 (2H, m, H Ar); 8.02 (1H, d, *J* = 7.5, H Ar); 8.14 (1H, d, *J* = 7.5, H Ar); 8.21 (1H, d, *J* = 7.5, H Ar); 8.44 (1H, d, *J* = 7.6, H Ar). ^{13}C NMR spectrum, δ, ppm: 13.9 ($\underline{C}H_3CH$=); 17.7 ($\underline{C}H_3$); 106.1 (CH=); 126.8, 127.3, 127.6, 128.5 (C Ar); 128.8, 128.9, 129.0, 129.1 (C Ph); 131.8 (C Ar); 132.8 (C Ph); 133.7, 133.9, 134.0, 135.0, 135.1 (C Ar); 135.2 (C Ph); 137.1 (C Ar); 137.3 (C–N); 144.9 ($CH_3\underline{C}H$=); 168.7 (C=N); 173.1 (COPh); 182.1 (CO); 182.4 (CO). Mass spectrum, *m*/*z* (I_{rel}, %): 439 $[M+H]^+$ (97). Found, %: C 71.31; H 4.01; N 6.41; S 7.59. $C_{26}H_{18}N_2O_3S$. Calculated, %: C 71.22; H 4.14; N 6.39; S 7.31.

***N*-[3-(4-Amino-9,10-dioxo-9,10-dihydroanthracen-1-yl)-4-methyl-1,3-thiazol-2(3H)-ylidene]benzamide (2c).** Yield 50%; mp 296-297°C. IR spectrum, ν, cm^{-1}: 3365, 3307 (NH_2), 1683, 1625 (C=O quinone), 1650 (C=O amide), 1450 (C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.98 (3H, s, CH_3); 6.89 (1H, s, CH=); 7.20-7.31 (3H, m, H Ar, NH_2); 7.38-7.41 (2H, m, H Ar); 7.49-7.57 (3H, m, H Ph); 7.73-7.81 (2H, m,

H Ph); 7.87-7.91 (2H, m, H Ar); 8.23 (1H, d, J = 7.6, H Ar). ^{13}C NMR spectrum, δ, ppm: 13.7 ($\underline{C}H_3CH$=); 107.2 (CH=); 114.5, 125.3, 126.1, 127.2 (C Ar); 128.1, 128.2, 129.3, 129.4 (C Ph); 130.1 (C–N); 130.9, 131.3 (C Ar); 132.3 (C Ph); 133.1, 133.2, 133.5, 133.8 (C Ar); 136.1 (C Ph); 139.8 ($CH_3\underline{C}H$=); 147.8 (C–NH_2); 169.7 (C=N); 174.5 (COPh); 183.1 (CO); 184.3 (CO). Mass spectrum, m/z (I_{rel}, %): 440 $[M+H]^+$ (73). Found, %: C 68.41; H 4.01; N 9.69; S 7.37. $C_{25}H_{17}N_3O_3S$. Calculated, %: C 68.32; H 3.90; N 9.56; S 7.30.

***N*-[3-(5-Amino-9,10-dioxo-9,10-dihydroanthracen-1-yl)-4-methyl-1,3-thiazol-2(3*H*)-ylidene]benzamide (2d)**. Yield 69%; mp 232-233°C. ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.97 (3H, s, CH_3); 6.92 (1H, s, CH=); 7.15-7.26 (5H, m, H Ar); 7.34-7.46 (2H, m, H Ph); 7.63-7.72 (3H, m, H Ph, NH_2); 7.83-7.91(1H, m, H Ar); 8.13-8.16 (1H, m, H Ar); 8.53 (1H, d, J = 8.4, H Ar). ^{13}C NMR spectrum, δ, ppm: 13.8 ($\underline{C}H_3CH$=); 106.8 (CH=); 111.9, 115.4, 120.1, 122.2, 123.7 (C Ar); 128.1, 129.2, 129.3, 129.4, 132.4 (C Ph); 132.9, 133.4, 135.0, 135.3, 135.7 (C Ar); 136.1 (C Ph); 138.2 (C–N); 139.3 ($CH_3\underline{C}H$=); 151.8 (C–NH_2); 168.2 (C=N); 174.5 (COPh); 183.6 (CO); 184.4 (CO). Mass spectrum, m/z (I_{rel}, %): 440 $[M+H]^+$ (82). Found, %: C 68.38; H 3.95; N 9.62; S 7.35. $C_{25}H_{17}N_3O_3S$. Calculated, %: C 68.32; H 3.90; N 9.56; S 7.30.

***N*-[3-(4-Benzamido-9,10-dioxo-9,10-dihydroanthracen-1-yl)-4-methyl-1,3-thiazol-2(3*H*)-ylidene]benzamide (2e).** Yield 48%; mp 198°C. IR spectrum, ν, cm^{-1}: 3345 (N–H), 1683, 1625 (C=O quinone), 1650, 1661 (C=O amide), 1450 (C=N). ^{1}H NMR spectrum, δ, ppm (J, Hz): 2.04 (3H, s, CH_3); 6.95 (1H, s, CH=); 7.31-7.40 (1H, m, H Ar); 7.72-8.27 (11H, m, H Ph, H Ar); 8.83-8.92 (2H, m, H Ar); 9.29-9.41 (2H, m, H Ar); 13.30 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 14.1 ($\underline{C}H_3CH$=); 106.3 (CH=); 118.2, 125.1, 126.5 (C Ar); 127.2, 127.3, 128.0, 128.1, 128.8, 128.9, 129.3, 129.4 (C Ph); 129.5, 130.3 (C Ar); 132.4, 132.5 (C Ph); 133.0 (C Ar); 133.2 (C–NH); 133.3 (C Ph); 133.4, 133.7, 134.3, 136.2 (C Ar); 136.0 (C Ph); 138.2 (C–N); 138.8 ($CH_3\underline{C}H$=); 165.7 (CO); 167.8 (C=N); 174.4 (COPh); 182.6 (CO); 184.5 (CO). Found, %: C 70.76; H 3.96; N 7.68; S 5.87. $C_{32}H_{21}N_3O_4S$. Calculated, %: C 70.70; H 3.89; N 7.73; S 5.90.

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