Synthesis and Spectral Properties of 4-Oxothiazolin-2-yl-[*N*-R_1-2-(*para*-R_2-phenyl)indol-3-yl] Hydrazones

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The preparation of several 4-oxothiazolin-2-yl-indol-3-yl hydrazones is described. The structure of all products was corroborated by ir, ^{1}H-nmr and mass spectrometry.

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There have been several reports concerning biological interest for indole and its derivatives. Some of these compounds are known to have activities such as anxyolitic [3], diuretic [4], cardiovascular [5] and other pharmacological properties [6,7]. Likewise, compounds possessing a 4-oxothiazoline moiety often exhibit an interesting spectrum of biological activities [8,9,10]. As a part of program directed towards the synthesis and spectral property determination of heterocyclic derivatives with possible pharmacological activity, we describe in this report the synthesis of compounds of general formula **IV** and **V** following the two steps indicated in Scheme 1.

The reaction of 4-phenylthiosemicarbazide with **I** in ethanol and acetic acid as the catalyst, gave the hydrazinecarbothioamides **II**. In the infrared spectra of **II** the appearance of bands at 3320, 3300 and 1200 cm^{-1} was consistent with the presence of an hydrazinecarbothioamide group [11]. In the ^{1}H-nmr spectra of **II** derivatives the presence of two downfield one-proton singlet at δ 10.9 and δ 9.2, which exchange upon introduction of deuterium ox-

Scheme 1

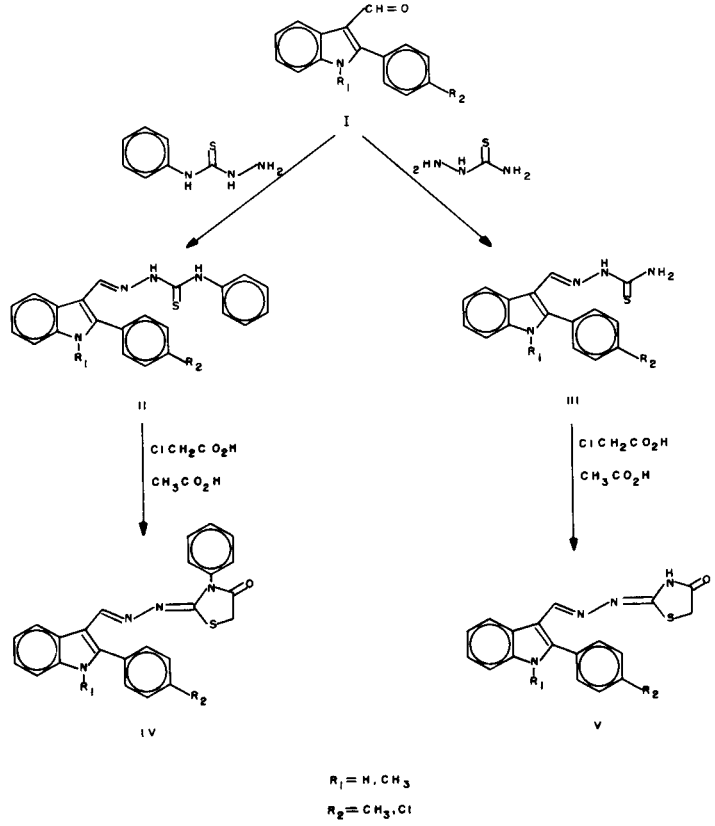

Table 1

Physical, Analytical and Spectral Data for the *N*-Phenyl-2-{[*N*-R_1-2(*p*-R_2 -Phenyl)-indol-3-yl]methylene} Hydrazinecarbothioamide II

Compound No.	R_1	R_2	Mp °C	Yield %	Molecular Formula	Analyses % C	H	Spectral Data
1	H	CH_3	190-192	80	$C_{23}H_{20}N_4S$	71.84 (71.80)	5.24 (5.22)	ir (nujol): 3420, 3320, 3300, 1200 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.9 (s, 1H), 9.2 (s, 1H), 8.85 (s, 1H), 8.15 (s, 1H), 7.8-7.0 (m, 13H), 2.45 (s, 3H); ms: M^+ m/z 384
2	H	Cl	192-194	79	$C_{22}H_{17}ClN_4S$	65.25 (65.21)	4.23 (4.22)	ir (nujol): 3410, 3320, 3300, 1200 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.8 (s, 1H), 9.8 (s, 1H), 8.85 (s, 1H), 8.2 (s, 1H), 7.9-7.0 (m, 13H); ms: M^+ m/z 404
3	CH_3	CH_3	195-197	78	$C_{24}H_{22}N_4S$	72.33 (72.30)	5.57 (5.55)	ir (nujol): 3250, 3150, 1200 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.8 (s, 1H), 9.1 (s, 1H), 8.2 (s, 1H), 7.8-7.0 (m, 13H), 3.65 (s, 3H), 2.45 (s, 3H); ms: M^+ m/z 398
4	CH_3	Cl	215-217	83	$C_{23}H_{19}ClN_4S$	65.94 (65.90)	4.57 (4.56)	ir (nujol); 3250, 3140, 1200 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.9 (s, 1H), 9.8 (s, 1H), 8.2 (s, 1H), 7.9-7.0 (m, 13H), 3.65 (s, 3H), ms: M^+ m/z 418

Table 2

Physical, Analytical and Spectral Data for the 2-{[*N*-R_1-2(*p*-(*p*-R_2-Phenyl)Phenyl)-indol-3-yl) Methylene} Hydrazinecarbothioamide III

Compound No.	R_1	R_2	Mp °C	Yield %	Molecular Formula	Analyses % C	H	Spectral Data
5	H	CH_3	298-300	69	$C_{17}H_{16}N_4S$	66.20 (66.18)	5.23 (5.21)	ir (nujol): 3420, 3320, 3200, 1180 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.94 (s, 1H), 8.9 (s, 1H), 8.1 (s, 1H), 7.6-7.0 (m, 8H), 3.2 (s, 2H), 2.4 (s, 3H); ms: M^+ m/z 308
6	H	Cl	220-222	60	$C_{16}H_{13}ClN_4S$	58.44 (58.40)	3.98 (3.97)	ir (nujol): 3420, 3315, 3100, 1200 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.0 (s, 1H), 8.9(s, 1H), 8.0 (s, 1H), 7.8-7.1 (m, 8H), 3.3 (s, 2H); ms: M^+ m/z 328
7	CH_3	CH_3	271-273	59	$C_{18}H_{18}N_4S$	67.05 (66.98)	5.63 (5.61)	ir (nujol): 3315, 3100, 1190 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.0 (s, 1H), 8.0 (s, 1H), 7.6-7.0 (m, 8H), 3.6 (s, 3H), 3.2 (s, 2H), 2.4 (s, 3H); ms: M^+ m/z 322
8	CH_3	Cl	218-220	76	$C_{17}H_{15}ClN_4S$	59.56 (59.50)	4.41 (4.40)	ir (nujol): 3320, 3110, 1195 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.8 (s, 1H), 8.2 (s, 1H), 7.7-7.1 (m, 8H) 3.6 (s, 3H); ms: M^+ m/z 342

Table 3

Physical, Analytical and Spectral Data for the 3-Aryl-4-oxothiazolin-2-yl[*N*-R_1-2-(*p*-R_2-Phenyl)-indol-3-yl] Hydrazones IV

Compound No.	R_1	R_2	Mp °C	Yield %	Molecular Formula	Analyses % C	H	Spectral Data
9	H	CH_3	193-195	71	$C_{25}H_{20}N_4OS$	70.73 (70.70)	4.75 (4.73)	ir (nujol): 3420, 1710 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.9 (s, 1H), 8.4 (s, 1H), 8.1-7.0 (m, 13H), 3.95 (s, 2H), 2.4 (s, 3H); ms: M^+ m/z 424
10	H	Cl	198-200	70	$C_{24}H_{17}ClN_4OS$	64.78 (64.74)	3.85 (3.84)	ir (nujol): 3400, 1705 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.8 (s, 1H), 8.2 (s, 1H), 8.0-7.0 (m, 13H), 3.9 (s, 2H); ms: M^+ m/z 444
11	CH_3	CH_3	196-198	77	$C_{26}H_{22}N_4OS$	71.21 (71.15)	5.06 (5.04)	ir (nujol): 1710 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.3 (s, 1H), 8.0-7.0 (m, 13H), 3.9 (s, 2H), 3.6 (s, 3H), 2.45 (s, 3H); ms: M^+ m/z 438
12	CH_3	Cl	217-219	71	$C_{25}H_{19}ClN_4OS$	65.42 (65.39)	4.17 (4.16)	ir (nujol): 1710 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.7 (s, 1H), 8.1-7.0 (m, 13H), 3.9 (s, 2H), 3.8 (s, 3H); ms: M^+ m/z 458

ide, confirmed the above assertion; other two downfield one-proton singlet at δ 8.8 and 8.2 were assigned to the proton joined to NH-indole framework and the methine proton of the imine group, respectively [12]. The aromatic protons in compounds **II** appeared as an unresolved multiplet at δ 7.0-7.9. Condensation of **I** with thiosemicarbazone in hot ethanol led to the hydrazine carbothioamides **III** in good yields. The latter also shown in their ir and ^{1}H-nmr spectra the characteristic signal due to the presence of the hydrazinecarbothioamide group in their framework (see Table 2). Treatment of carbothioamides **II** or **III** with chloroacetic-acetic acid [8] and sodium acetate

Table 4

Physical, Analytical and Spectral Data for the 4-Oxothiazolin-2-yl [*N*-R_1-2-(*p*-R_2-Phenyl)-indol-3-yl] Hydrazones **V**

Compound No.	R_1	R_2	Mp °C	Yield %	Molecular Formula	Analyses % C	H	Spectral Data
13	H	CH_3	135-137	76	$C_{19}H_{16}N_4OS$	65.49 (65.45)	4.63 (4.61)	ir (nujol): 3400, 3200, 1710 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.0 (s, 1H), 8.8 (s, 1H), 8.3 (s, 1H), 8.1-7.0 (m, 8H), 3.95 (s, 2H), 2.4 (s, 3H), ms: M^+ m/z 348
14	H	Cl	178-180	72	$C_{18}H_{13}ClN_4OS$	58.61 (58.59)	3.55 (3.54)	ir (nujol): 3400, 3200, 1705cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.1 (s, 1H), 8.9 (s, 1H), 8.4 (s, 1H), 8.2-7.2 (m, 8H), 3.9 (s, 2H); ms: M^+ m/z 368
15	CH_3	CH_3	152-154	70	$C_{20}H_{18}N_4OS$	66.27 (66.23)	5.00 (4.98)	ir (nujol): 3200, 1710 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.0 (s, 1H), 8.4 (s, 1H), 8.0-7.0 (m, 8H), 3.9 (s, 2H), 3.6 (s, 3H), 2.4 (s, 3H); ms: M^+ m/z 362
16	CH_3	Cl	220-222	79	$C_{19}H_{15}ClN_4OS$	59.60 (59.57)	3.95 (3.93)	ir (nujol): 3200, 1710 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.0 (s, 1H), 8.4 (s, 1H), 8.1-7.1 (m, 8H), 3.9 (s, 2H), 3.6 (s, 3H); ms: M^+ m/z 382

in ethanol afforded **IV** and **V**, respectively (Scheme 1). In the infrared spectra of compounds **IV**, a characteristically band for the thiazolinone group [13] was present (1710 cm^{-1}). In the ^1H-nmr spectra of derivatives **IV** the presence of a two proton singlet at δ 3.95 confirmed the thiazolinone group; a downfield one-proton singlet at δ 8.3 was assigned to the methine proton of the imine group. Likewise a three proton singlet at δ 3.6 was assigned to the *N*-methyl protons in the compounds with $R_1 = CH_3$-. The aromatic protons in compounds **IV** appeared as unresolved multiplet at δ 7.0-8.1.

We found that the ir and ^1H-nmr spectra of compounds **V** are similar to **IV** derivatives and therefore they are not discussed in detail (Table 4).

EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded on a Nicolet FT-55X spectrophotometer. The ^1H-nmr spectra were recorded on a Varian FT-80 spectrometer operating at 80 MHz, in hexadeuteriodimethyl sulfoxide solution containing tetramethylsilane as the internal standard with chemical shifts (δ) expressed downfield from TMS. Mass spectra were obtained with a Hewlett Packard 59854-A quadropole spectrometer. All compounds were synthesized following reported procedures [8]. Analytical and spectral data on the new compounds are recorded on Tables 1-4.

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