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SYNTHESIS OF 2,5-DIHYDROISOTHIAZOLE DERIVATIVES. 2*. 3-ARYL(HETARYL)-SUBSTITUTED 2-ALKYL-5-ARYLIMINO-2,5-DIHYDROISOTHIAZOLES

I. Skrastiņa[1], A. Baran[1], D. Muceniece[1], and J. Popelis[1]**

A series of new 2-alkyl-5-arylimino-2,5-dihydroisothiazoles, substituted at position 3 with aryl and hetaryl groups and not substituted at position 4 was prepared by oxidative cyclization of N-arylamides of 3-alkylaminoprop-2-enethioic acids. The formation of the starting thioanilides was investigated by reacting the respective N-alkylimines of acetophenones with isothiocyanates. The main by-products were identified and characterized.

Keywords: 2-alkyl-3-aryl(hetaryl)-5-arylimino-2,5-dihydroisothiazole, *N*-arylamides of 3-alkylamino-3-aryl(hetaryl)prop-2-enethioic acid, oxidative cyclization.

N-Arylanilides of 3-amino-2-ene- and 3-oxocarboxylic and thiocarboxylic acids are convenient precursors for the synthesis of various biologically active heterocyclic systems, including derivatives of pyrrolidine [2, 3], pyridine [4], benzothiazole [5], dithiolane [6], dithiazole, and isothiazole (1,2-thiazole) [2, 7]. For instance, the oxidative cyclization of 3-aminoprop-2-enethioic acid amides leads to the formation of isothiazole-5(2*H*)-imines [8-11]. Despite the apparent simplicity of the method and the availability of the starting compounds, the reaction often gives variable results, producing many by-products besides the target isothiazoles [8, 9, 12, 13]. Probably due to this reason, partially hydrogenated isothiazoles remain a little known class of compounds (see, for example, the reviews [14, 15]). Our literature search for these compounds identified only approximately thirty publications, of which only a few appeared after the year 1990 [16-19].

We have previously obtained 2-alkyl-5-arylimino-2,5-dihydroisothiazole derivatives containing a methyl group at position 3, as well as a benzoyl or ester group at position 4 [1]. In a continuation of investigations towards the synthesis and the study of biological activity of 2-alkyl-5-arylimino-2,5-dihydroisothiazole derivatives, we synthesized a range of new compounds of this class, containing aryl and hetaryl substituents at position 3, and having no substituents at position 4.

We planned to prepare the target compounds from acetophenones or the acetylpyridines **1a-e** by converting them to the respective imines **A** through reactions with primary alkylamines [20, 21]. The obtained imines reacted with the isothiocyanates **2a-i** forming the thioamides **3a-u** that could be converted to the target dihydroisothiazoles **4a-u** by oxidative cyclization according to known methods [9, 22-24].

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*For Communication 1, see [1].

**To whom correspondence should be addressed, e-mail: ingrida@osi.lv.

[1] Latvian Institute of Organic Synthesis, 21 Aizkraukles St., Riga LV-1006, Latvia.

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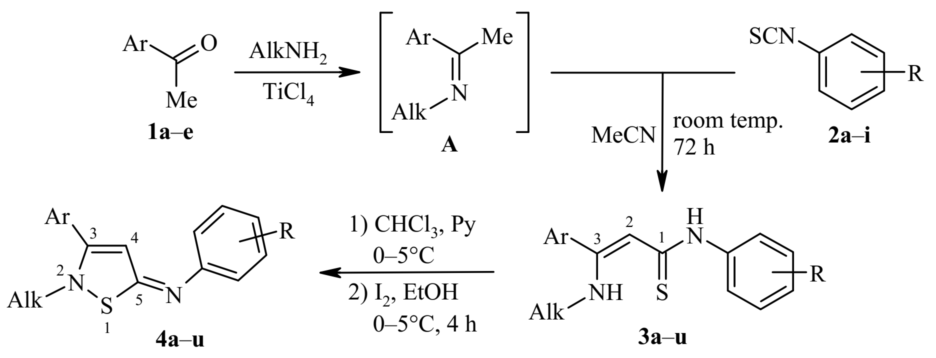
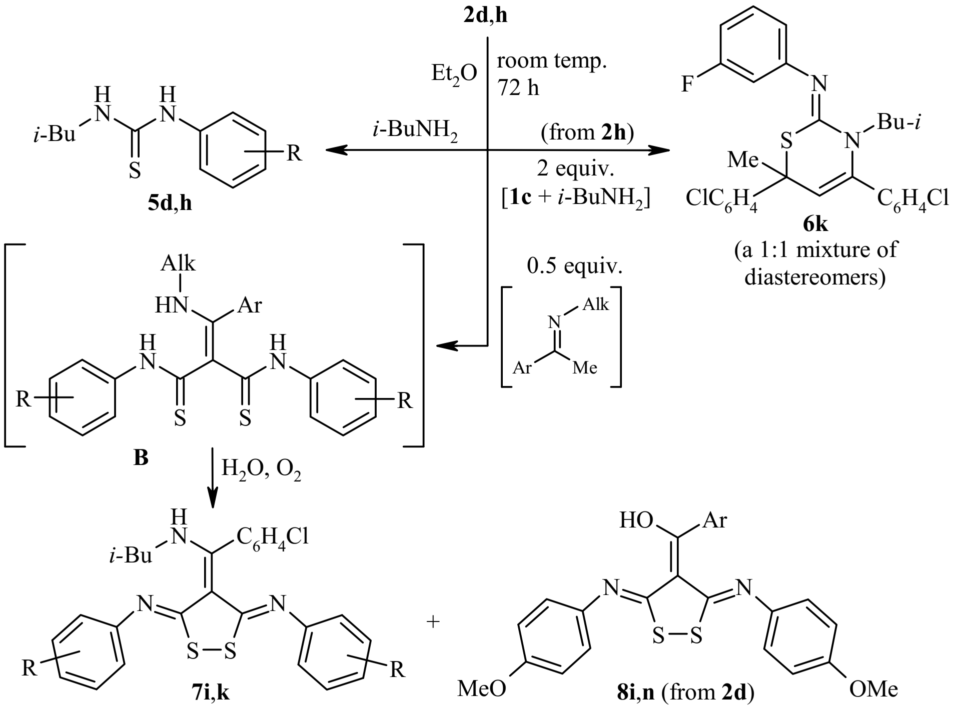


1 a Ar = Ph, **b** Ar = 4-$MeOC_6H_4$, **c** Ar = 4-ClC_6H_4, **d** Ar = 4-Py, **e** Ar = 3-Py; **2 a** R = H, **b** R = 4-Me, **c** R = 3-Me, **d** R = 4-MeO, **e** R = 4-Me_2N, **f** R = 4-Cl, **g** R = 4-F, **h** R = 3-F, **i** R = 3,4-Cl_2; **3,4 a**–**f**,**l**–**u** Alk = *n*-Pr; **g**,**h**,**j** Alk = *n*-Bu; **i**,**k** Alk = *i*-Bu; **a** Ar = Ph, R = 4-Cl; **b** Ar = Ph, R = 4-F; **c** Ar = 4-$MeOC_6H_4$, R = 4-Me; **d** Ar = 4-$MeOC_6H_4$, R = 4-MeO; **e** Ar = 4-$MeOC_6H_4$, R = 4-F; **f** Ar = 4-$MeOC_6H_4$, R = 3-F; **g** Ar = 4-ClC_6H_4, R = H; **h** Ar = 4-ClC_6H_4, R = 4-Me; **i** Ar = 4-ClC_6H_4, R = 4-MeO; **j** Ar = 4-ClC_6H_4, R = 4-Cl; **k** Ar = 4-ClC_6H_4, R = 3-F; **l** Ar = 4-ClC_6H_4, R = 3,4-Cl_2; **m** Ar = 4-Py, R = 4-Me; **n** Ar = 4-Py, R = 4-MeO; **o** Ar = 4-Py, R = 4-Me_2N; **p** Ar = 4-Py, R = 4-Cl; **q** Ar = 4-Py, R = 3-F; **r** Ar = 4-Py, R = 3,4-Cl_2; **s** Ar = 3-Py, R = 3-F; **t** Ar = 3-Py, R = 3-Me; **u** Ar = 3-Py, R = 4-MeO

The first attempts of "traditional" synthesis of the imines **A** showed that this process was slow and did not go to completion even after 1 week at room temperature, according to the TLC and LC/MS data [20]. Using the obtained reaction mixture (with 60-70% imine content according to chromatography) in the further stages of synthesis resulted in the formation of not only the target compounds **3** and **4**, but also a range of minor products **5-8**, which were isolated and characterized by NMR spectroscopy and X-ray structural analysis (Fig. 1 and 2).



5 d R = 4-MeO, **h** R = 3-F; **7 i** R = 4-MeO, **k** R = 3-F; **8 i** Ar = 4-ClC_6H_4, **n** Ar = 4-Py

TABLE 1. The Reaction Conditions and Yields of 4-Methoxyacetophenone Propylimine

Amount of amine, equiv.	Solvent, condensing agent*	Reaction duration, h	Imine yield*2, %
2.0	PhH, cat. AcOH	340	13
5.0	PhH, cat. AcOH	48	34
		72	54
10.0	PhH, cat. AcOH	48	67
		72	75
2.0	PhH, mol. sieves 4 Å, activated at 120°C	24	3
		72	13
2.0	$CHCl_3$, $TiCl_4$ (2.0 equiv.)	24	68
		48	91
2.0	$CHCl_3$, Ti(O-*i*-Pr)$_4$ (2.0 equiv.)	24	46
		48	84
		72	87
2.0	$CHCl_3$, polyphosphoric acid (2.0 equiv.)	24	<1
		48	<1
2.0	$CHCl_3$, $POCl_3$ (2.0 equiv.)	24	<1
		48	<1

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*All reactions were performed at room temperature.

*2The yield of the imine was determined by LC/MS without isolation from the reaction mixture.

A review of the available literature about the synthesis of imines identified a multitude of predominantly acidic reagents that acted as scavengers of water [25]. The most common of these reagents were used in the synthesis of imines for this project, as presented in the Table 1. The propylimine of 4-methoxy-acetophenone was selected as the model compound.

The Table 1 shows that titanium(IV) reagents were superior for achieving the condensation reaction producing the target imine: the product yield reached ~90% after 48-72 h. The imine content in the reaction mixture was nearly as high after 72 h at room temperature when a large excess of the amine (≥10 equiv.) was used. Heating the reaction mixture to 40-50°C did not significantly accelerate the process.

The further experiments of imine synthesis for this project were performed with $TiCl_4$ (2.0 equiv.) with subsequent quenching of the excess condensing agent with a 10% aqueous NaOH solution by analogy to the methods [21, 26]. The product isolated under these conditions contained about 90% of the target derivative and 10% of the starting acetophenone, the presence of which did not interfere with the subsequent stages.

The interaction of the obtained imines **A** with the isothiocyanates **2a-i** proceeded without forming the previously observed *N*-alkyl-*N'*-arylthioureas **5**. The appearance of the latter in the preliminary experiments was probably caused by the presence of significant quantities of unreacted primary amine in the reaction mixture, which then easily reacted with isothiocyanates. The combined content of the by-products **6** and **B** was unchanged according to LC/MS data, and was not higher than 15% of the amount of the target thioamides **3a-u**, which were isolated in moderate yields (62-78%, Table 2).

The formation of the thiazines analogous to compound **6** occurred by interaction of one isothiocyanate molecule with two imine molecules as a formal [4+2] cycloaddition [27] of isothiocyanate (dienophile) to the imine dimerization product (azabutadiene), or as a pericyclic process [28]. Compound **6k** was obtained as a 1:1 mixture of diastereomers according to NMR and X-ray structural analysis data (Table 3, Fig. 1*a*), and the unit cell consisted of two adjacent molecules of the opposite diastereomers. The derivatives **7i**,**k** and **8i**,**n** were formed by the interaction of two isocyanate molecules with one imine molecule. The intermediate dithiol **B** (not isolated, but detected by LC/MS) underwent oxidative cyclization into the 1,2-dithiolane [6, 29] upon contact with air. The structures of compounds **7k** and **8n** were also confirmed by NMR spectroscopy and X-ray structural analysis (Table 3, Fig. 1*b*,*c*).

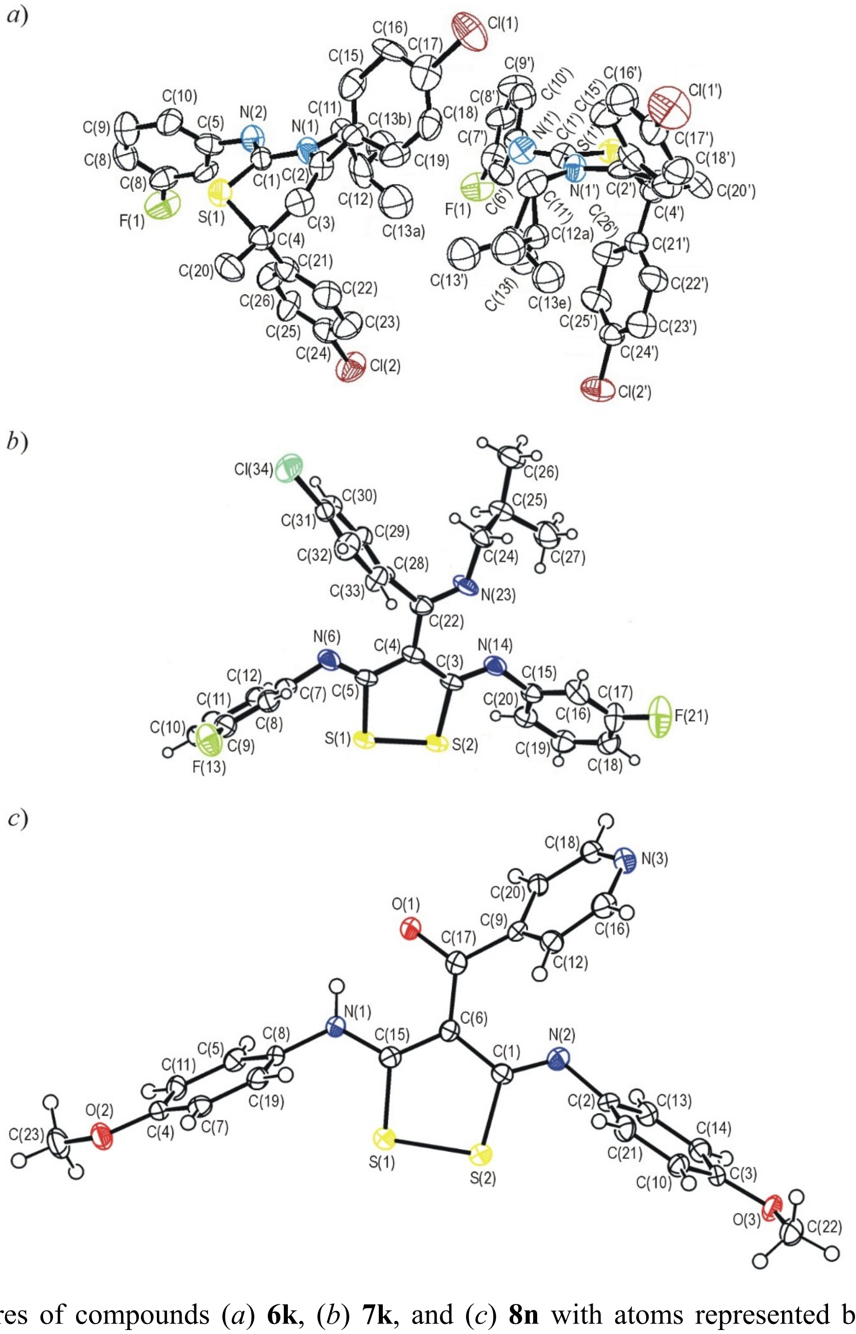

Fig. 1. The structures of compounds (*a*) **6k**, (*b*) **7k**, and (*c*) **8n** with atoms represented by thermal vibration ellipsoids of 50% probability.

Remarkably, the cyclization of the thioanilides **3a-u** into the dihydroisothiazoles **4a-u** proceeded relatively smoothly. The sulfur atom of the starting compounds was oxidized under mild conditions by the action of molecular iodine or bromine, after which the mixture was treated with a saturated Na_2CO_3 solution according to the methods [9, 12]. The target compounds were obtained in 82-96% yields.

The structures of the obtained 3-amino-3-arylprop-2-enethioamides **3a-u** were confirmed by NMR spectroscopy (Table 3) and X-ray structural analysis. All of the obtained derivatives without an exception existed only in the *cis*-enamine form due to the strong NH···S=C hydrogen bonding between the enamine and thioamide groups. The proton of the enamine fragment gave an NMR signal in the downfield region at 11.68-11.98 ppm.

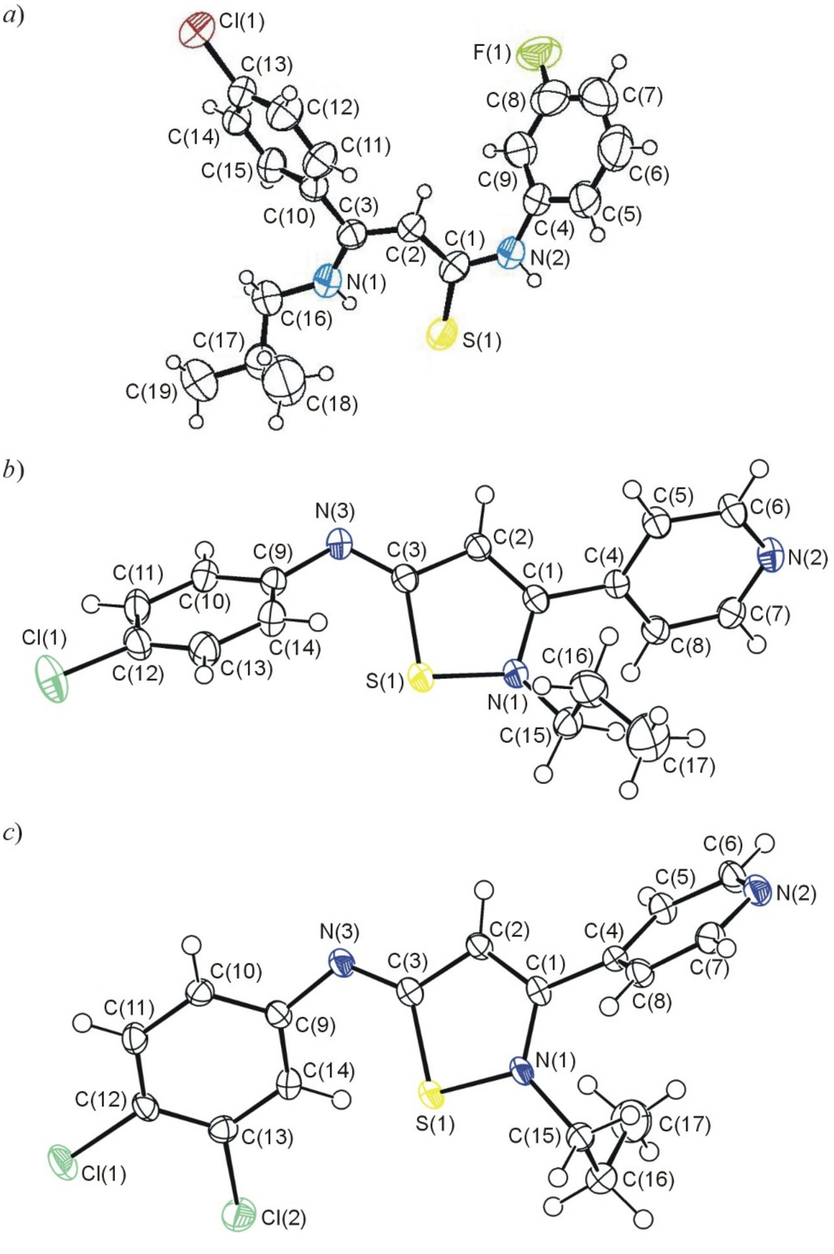

Fig. 2. The structures of compounds (*a*) **3k**, (*b*) **4p**, and (*c*) **4r** with atoms represented by thermal vibration ellipsoids of 50% probability.

The structures of the dihydroisothiazoles **4a-u** were also in agreement with the ^{1}H and ^{13}C NMR spectroscopy data (Table 3). The ^{1}H NMR signals due to the protons at position 4 of the isothiazole ring appeared at 6.04-6.10 ppm in the case of the aryl derivatives, and 6.10-6.21 ppm in the case of the hetaryl derivatives. The ^{13}C NMR signals of the isothiazole C-3, C-4, and C-5 atoms were observed at 159.5-163.7, 107.3-110.6, and 163.8-167.7 ppm, respectively. The structures of the products **4p**,**r** were also confirmed by X-ray structural analysis (Fig. 2). It was established that the imine double bond had a (*Z*)-configuration, the aromatic rings were at sterically favored positions, and were rotated at an angle relative to the isothiazole ring plane.

TABLE 2. The Physicochemical Characteristics of the Synthesized Compounds

Com-pound	Empirical formula	Found, % Calculated, %			Mp*, °C	Yield, %	Color
		C	H	N			
1	2	3	4	5	6	7	8
3a	$C_{18}H_{19}ClN_2S$	65.02 65.34	5.51 5.79	8.41 8.47	142-145	73	Light-yellow
3b	$C_{18}H_{19}FN_2S$	68.71 68.76	5.97 6.09	8.79 8.91	99-101	78	Light-yellow
3c	$C_{20}H_{24}N_2OS$	70.25 70.55	7.08 7.10	8.22 8.23	173-176	62	Light-yellow
3d	$C_{20}H_{24}N_2O_2S$	67.33 67.39	6.83 6.79	7.81 7.86	176-179	72	Light-yellow
3e	$C_{19}H_{21}FN_2OS$	66.15 66.25	6.08 6.15	8.02 8.13	173-175	64	Light-yellow
3f	$C_{19}H_{21}FN_2OS$	66.38 66.25	6.29 6.15	8.06 8.13	110-112	73	Light-yellow
3g	$C_{19}H_{21}ClN_2S$	66.08 66.17	6.16 6.14	8.04 8.12	143-145	66	Light-yellow
3h	$C_{20}H_{23}ClN_2S$	66.69 66.93	6.22 6.46	7.74 7.80	96-98	65	Light-yellow
3i	$C_{20}H_{23}ClN_2OS$	64.02 64.07	6.16 6.18	7.51 7.47	139-141	63	Yellow
3j	$C_{19}H_{20}Cl_2N_2S$	60.10 60.16	5.23 5.31	7.37 7.38	159-160	71	Light-yellow
3k	$C_{19}H_{20}FClN_2S$	62.90 62.89	5.66 5.56	7.66 7.72	149-151	68	Light-yellow
3l	$C_{18}H_{17}Cl_3N_2S$	54.25 54.08	4.22 4.29	6.94 7.01	159-161	70	Light-yellow
3m	$C_{18}H_{21}N_3S$	69.31 69.42	6.98 6.80	13.07 13.49	189-191	67	Yellow
3n	$C_{18}H_{21}N_3OS$	65.69 66.03	6.54 6.46	12.59 12.83	151-154	71	Light-yellow
3o	$C_{19}H_{24}N_4S$	67.16 67.02	7.12 7.11	16.38 16.45	172-174	62	Yellow
3p	$C_{17}H_{18}ClN_3S$	61.13 61.53	5.46 5.47	12.57 12.66	179-181	63	Light-yellow
3q	$C_{17}H_{18}FN_3S$	64.74 64.74	5.70 5.75	13.19 13.32	137-139	67	Light-yellow
3r	$C_{17}H_{17}Cl_2N_3S$	55.70 55.74	4.63 4.68	11.36 11.47	152-155	74	Yellow
3s	$C_{17}H_{18}FN_3S$	65.04 64.74	5.81 5.75	13.30 13.32	117-119	65	Light-yellow
3t	$C_{18}H_{21}N_3S$	69.46 69.42	6.76 6.80	13.44 13.49	122-124	69	Yellow
3u	$C_{18}H_{21}N_3OS$	65.84 66.03	6.57 6.46	12.71 12.83	156-158	64	Light-yellow
4a	$C_{18}H_{17}ClN_2S$	65.75 65.73	5.20 5.21	8.53 8.51	87-89	90	Yellow
4b	$C_{18}H_{17}FN_2S$	68.74 69.20	5.37 5.49	8.87 8.97	124-126	83	Yellow
4c	$C_{20}H_{22}N_2OS$	70.79 70.97	6.50 6.55	8.25 8.28	105-107	86	Yellow
4d	$C_{20}H_{22}N_2O_2S$	67.64 67.77	6.29 6.26	7.80 7.90	116-119	89	Orange
4e	$C_{19}H_{19}FN_2OS$	66.55 66.64	5.56 5.59	8.12 8.18	106-108	88	Light-yellow
4f	$C_{19}H_{19}FN_2OS$	66.78 66.64	5.63 5.59	8.14 8.18	89-91	82	Yellow
4g	$C_{19}H_{19}ClN_2S$	66.41 66.55	5.49 5.59	8.18 8.17	111-114	88	Orange
4h	$C_{20}H_{21}ClN_2S$	67.25 67.30	5.88 5.93	7.81 7.85	99-100	87	Light-yellow
4i	$C_{20}H_{21}ClN_2OS$	64.39 64.41	5.61 5.67	7.50 7.51	124-126	84	Light-yellow
4j	$C_{19}H_{18}Cl_2N_2S$	60.58 60.48	4.79 4.81	7.40 7.42	125-126	90	Light-yellow

TABLE 2 (continued)

1	2	3	4	5	6	7	8
4k	$C_{19}H_{18}ClFN_2S$	63.20 63.24	4.97 5.03	7.72 7.76	115-118	87	Orange
4l	$C_{18}H_{15}Cl_3N_2S$	54.37 54.35	3.75 3.80	6.92 7.04	138-141	94	Light-yellow
4m	$C_{18}H_{19}N_3S$	69.81 69.87	5.99 6.19	13.46 13.58	144-146	87	Yellow
4n	$C_{18}H_{19}N_3OS$	66.49 66.43	5.67 5.89	12.86 12.91	130-132	84	Yellowish brown
4o	$C_{19}H_{22}N_4S$	67.50 67.42	6.69 6.55	16.63 16.55	132-135	82	Orange
4p	$C_{17}H_{16}ClN_3S$	61.90 61.90	4.73 4.89	12.66 12.74	127-129	89	Yellow
4q	$C_{17}H_{16}FN_3S$	54.91 55.15	5.03 5.15	13.28 13.41	104-106	90	Orange
4r	$C_{17}H_{15}Cl_2N_3S$	56.06 56.05	3.89 4.15	11.46 11.53	150-152	89	Light-yellow
4s	$C_{17}H_{16}FN_3S$	65.37 65.15	5.29 5.15	13.33 13.41	105-107	82	Light-yellow
4t	$C_{18}H_{19}N_3S$	69.76 69.87	6.24 6.19	13.50 13.58	60-62	85	Light-yellow
4u	$C_{18}H_{19}N_3OS$	66.43 66.43	5.91 5.89	12.87 12.91	63-65	86	Yellow
5d	$C_{12}H_{18}N_2OS$	60.49 60.47	7.79 7.61	11.68 11.75	119-121	20	White
5h	$C_{11}H_{15}FN_2S$	58.43 58.38	6.65 6.68	12.26 12.28	66-68	23	White
6k	$C_{27}H_{25}Cl_2FN_2S$	65.13 64.93	4.97 5.05	6.57 5.61	107-109	14	White
7i	$C_{28}H_{28}ClN_3O_2S_2$	62.54 62.50	5.33 5.24	7.57 7.81	218-220	1	Light-yellow
7k	$C_{26}H_{22}ClF_2N_3S_2$	65.90 60.75	4.30 4.31	8.11 8.17	147-149	4	Light-yellow
8i	$C_{24}H_{19}ClN_2O_3S_2$	59.81 59.68	4.13 3.97	5.66 5.80	172-174	3	Yellow
8n	$C_{23}H_{19}N_3O_3S_2$	61.32 61.45	4.30 4.26	9.26 9.35	201-203	6	Yellow

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*Solvents for recrystallization: Et_2O (compounds **3s-u**, **5d**), H_2O (compound **5h**), hexane (compounds **6k**, **7k**), CH_2Cl_2 (compound **8n**), MTBE (the rest of the compounds)

Thus, we have described the preparation of a series of new 3-aryl(hetaryl)-substituted 2-alkyl-5-arylimino-2,5-dihydroisothiazoles by oxidative cyclization of the respective 3-substituted anilides of 3-alkylaminoprop-2-enethioic acids. The reaction leading to the formation of the starting thioamides was investigated, and the most significant by-products were isolated and characterized. A study of the cytotoxic properties of the obtained isothiazoles is planned.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were acquired on a Varian 400-MR instrument (400 and 100 MHz, respectively) in $CDCl_3$, the residual solvent protons were used as internal standard (7.27 ppm for ^1H nuclei, 77.0 ppm for ^{13}C nuclei). The signals in certain cases were assigned by using homo- and heteronuclear 2D NMR experiments: COSY, NOESY, HMBC, and HSQC. Mass spectra were recorded using an HPLC-MS equipment that consisted of an Acquity UPLC system (Waters)-Q-TOF (Micromass) with a Waters Xbridge C18 column (3.5 µm, 2.1×50 mm), 0.6 ml/min flow rate, gradient elution with MeCN–HCOOH (0.1%) in water, electrospray ionization,

TABLE 3. Spectral Characteristics of the Synthesized Compounds

Compound	^{1}H NMR spectrum, δ, ppm (J, Hz)	^{13}C NMR spectrum, δ, ppm (J_{C-F}, Hz)	Mass spectrum, m/z $[M+H]^+$
1	2	3	4
3a	0.97 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.61 (2H, sext, J = 7.3, $CH_2C\underline{H}_2Me$); 3.15 (2H, dt, J = 6.7, J = 6.3, $NHC\underline{H}_2$); 5.31 (1H, s, =CH–CS); 7.19-7.30 (6H, m, H Ar); 7.36-7.42 (3H, m, H Ar); 7.55 (1H, br. s, CSNH); 11.93 (1H, br. s, $N\underline{H}CH_2$)	11.5; 23.8; 47.0; 95.0; 125.9 (2C); 127.3 (2C); 128.5 (2C); 129.2 (2C); 129.3; 130.9; 136.9; 137.5; 165.8; 186.2	331
3b	0.98 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.62 (2H, sext, J = 7.3, $CH_2C\underline{H}_2Me$); 3.16 (2H, dt, J = 6.8, J = 6.1, $NHC\underline{H}_2$); 5.41 (1H, s, =CH–CS); 6.84 (1H, dddd, J = 8.4, J = 8.3, J = 2.5, J = 0.7, H-4 Ar); 7.04 (1H, dd, J = 8.0, J = 1.7, H-6 Ar); 7.10 (1H, ddd, J = 10.2, J = 2.3, J = 2.2, H-2 Ar); 7.26 (1H, ddd, J = 8.2, J = 8.2, J = 6.2, H-5 Ar); 7.28-7.32 (2H, m, H Ph); 7.37–7.43 (3H, m, H Ph); 7.60 (1H, br. s, CSNH); 11.98 (1H, br. s, $N\underline{H}CH_2$)	11.5; 23.7; 47.0; 95.2; 111.5 (d, ^2J = 23.7); 112.3 (d, ^2J = 21.2); 119.5 (d, ^4J = 1.8); 127.4 (2C); 128.5 (2C); 129.3; 130.2 (d, ^3J = 9.2); 136.8; 140.6 (d, ^3J = 9.9); 162.8 (d, ^1J = 246.5); 166.0; 186.0	315
3c	0.98 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.61 (2H, sext, J = 7.3, $CH_2C\underline{H}_2Me$); 2.31 (3H, s, $C_6H_4C\underline{H}_3$); 3.17 (2H, dt, J = 6.8, J = 6.2, $NHC\underline{H}_2$); 3.82 (3H, s, OCH_3); 5.34 (1H, s, =CH–CS); 6.89 (2H, d, J = 8.7, H ArOMe); 7.11 (2H, d, J = 8.7, H ArMe); 7.14 (2H, d, J = 8.7, H ArMe); 7.21 (2H, d, J = 8.7, H ArOMe); 7.56 (1H, br. s, CSNH); 11.82 (1H, br. s, $N\underline{H}CH_2$)	11.6; 20.9; 23.8; 47.0; 55.2; 94.6; 113.7 (2C); 124.9 (2C); 129.0 (2C); 129.4; 129.7 (2C); 135.6; 136.4; 160.2; 165.4; 186.0	341
3d	0.97 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.61 (2H, sext, J = 7.2, $CH_2C\underline{H}_2Me$); 3.16 (2H, dt, J = 6.7, J = 6.3, $NHC\underline{H}_2$); 3.78 (3H, s, OCH_3) 3.82 (3H, s, OCH_3); 5.22 (1H, s, =CH–CS); 6.84 (2H, d, J = 8.9, H NAr); 6.88 (2H, d, J = 8.7, H 3-Ar); 7.17 (2H, d, J = 8.9, H NAr); 7.20 (2H, d, J = 8.7, H 3-Ar); 7.50 (1H, br. s, CSNH); 11.78 (1H, br. s, $N\underline{H}CH_2$)	11.6; 23.8; 47.0; 55.3; 55.4; 94.4; 113.7 (2C); 114.3 (2C); 126.9 (2C); 129.0 (2C); 129.5; 131.9; 157.7; 160.2; 165.3; 186.5	357
3e	0.97 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.61 (2H, sext, J = 7.2, $CH_2C\underline{H}_2Me$); 3.18 (2H, dt, J = 6.7, J = 6.2, $NHC\underline{H}_2$); 3.82 (3H, s, OCH_3); 5.24 (1H, s, =CH–CS); 6.90 (2H, d, J = 8.6, H ArOMe); 7.01 (2H, dd, J = 8.5, J = 8.5, H-3,5 ArF); 7.17-7.25 (4H, m, H Ar); 7.51 (1H, br. s, CSNH); 11.85 (1H, br. s, $N\underline{H}CH_2$)	11.5; 23.8; 47.1; 55.3; 94.7; 113.8 (2C); 115.9 (2C, d, ^2J = 22.6); 127.1 (2C, d, ^3J = 8.2); 128.9 (2C); 129.2; 135.0; 159.3; 160.5 (d, ^1J = 246.0); 165.6; 186.4	345
3f	0.98 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.63 (2H, sext, J = 7.2, $CH_2C\underline{H}_2Me$); 3.20 (2H, dt, J = 6.8, J = 6.0, $NHC\underline{H}_2$); 3.83 (3H, s, OCH_3); 5.43 (1H, s, =CH–CS); 6.84 (1H, dddd, J = 8.4, J = 8.4, J = 2.5, J = 0.8, H-4 ArF); 6.92 (2H, d, J = 8.8, H ArOMe); 7.03 (1H, dd, J = 8.0, J = 1.7, H-6 ArF); 7.09 (1H, ddd, J = 10.2, J = 2.3, J = 2.2, H-2 ArF); 7.24 (2H, d, J = 8.8, H ArOMe); 7.26 (1H, ddd, J = 8.4, J = 8.2, J = 6.4, H-5 ArF); 7.54 (1H, br. s, CSNH); 11.95 (1H, br. s, $N\underline{H}CH_2$)	11.5; 23.8; 47.1; 55.3; 95.4; 111.4 (d, ^2J = 23.8); 112.2 (d, ^2J = 21.2); 113.9 (2C); 119.7 (d, ^4J = 2.4); 128.9 (2C); 129.1; 130.2 (d, ^3J = 9.3); 140.6 (d, ^3J = 9.9); 160.4; 162.8 (d, ^1J = 246.4); 166.0; 185.6	345
3g	0.89 (3H, t, J = 7.3, $(CH_2)_3C\underline{H}_3$); 1.41 (2H, sext, J = 7.3, $(CH_2)_2C\underline{H}_2Me$); 1.57 (2H, quint, J = 7.3, $NCH_2C\underline{H}_2Et$); 3.15 (2H, dt, J = 6.8, J = 6.1, $NHC\underline{H}_2$); 5.31 (1H, s, =CH–CS); 7.15-7.20 (1H, m, H-4 Ph); 7.22 (2H, d, J = 8.5, H Ar); 7.24-7.27 (2H, m, H-2,6 Ph); 7.30-7.38 (4H, m, H Ar, H-3,5 Ph); 7.69 (1H, br. S, CSNH); 11.84 (1H, br. S, $N\underline{H}CH_2$)	13.6; 20.0; 32.5; 44.9; 94.6; 124.8 (2C); 125.9; 128.8 (2C); 128.8 (2C); 129.2 (2C); 135.3; 135.4; 138.8; 164.2; 186.6	345
3h	0.89 (3H, t, J = 7.3, $(CH_2)_3C\underline{H}_3$); 1.40 (2H, sext, J = 7.3, $(CH_2)_2C\underline{H}_2Me$); 1.56 (2H, quint, J = 7.2, $NCH_2C\underline{H}_2Et$); 2.31 (3H, s, $C_6H_4C\underline{H}_3$) 3.13 (2H, dt, J = 6.7, J = 6.1, $NHC\underline{H}_2$); 5.25 (1H, s, =CH–CS); 7.12 (4H, s, H ArMe); 7.21 (2H, d, J = 8.5, H ArCl); 7.36 (2H, d, J = 8.5, H ArCl); 7.63 (1H, br. s, CSNH); 11.79 (1H, br. s, $N\underline{H}CH_2$)	13.6; 20.0; 21.0; 32.5; 44.9; 94.4; 124.9 (2C); 128.7 (2C); 128.9 (2C); 129.7 (2C); 135.2; 135.5; 135.9; 136.2; 164.0; 186.8	359

TABLE 3 (continued)

1	2	3	4
3i	0.96 (6H, d, J = 6.7, $\mathrm{CH(C\underline{H}_3)_2}$); 1.82 (1H, sept, J = 6.6, $\mathrm{C\underline{H}Me_2}$); 2.97 (2H, t, J = 6.3, $\mathrm{NHC\underline{H}_2}$); 3.79 (3H, s, $\mathrm{OCH_3}$); 5.15 (1H, s, =CH–CS); 6.85 (2H, d, J = 8.9, H ArOMe); 7.16 (2H, d, J = 8.8, H ArOMe); 7.19 (2H, d, J = 8.4, H ArCl); 7.35 (2H, d, J = 8.4, H ArCl); 7.57 (1H, br. s, CSNH); 11.80 (1H, br. s, $\mathrm{N\underline{H}CH_2}$)	20.2 (2C); 29.4; 52.9; 55.4; 94.3; 114.3 (2C); 127.0 (2C); 128.7 (2C); 128.9 (2C); 131.7; 135.1; 135.6; 157.9; 164.1; 187.2	375
3j	0.90 (3H, t, J = 7.3, $\mathrm{(CH_2)_3C\underline{H}_3}$); 1.39 (2H, sext, J = 7.3, $\mathrm{(CH_2)_2C\underline{H}_2Me}$); 1.57 (2H, quint, J = 7.2, $\mathrm{NCH_2C\underline{H}_2Et}$); 3.16 (2H, dt, J = 6.6, J = 6.4, $\mathrm{NHC\underline{H}_2}$); 5.24 (1H, s, =CH–CS); 7.20–7.24 (4H, m, H Ar); 7.29 (2H, d, J = 8.7, H Ar); 7.38 (2H, d, J = 8.3, H Ar); 7.55 (1H, br. s, CSNH); 11.86 (1H, br. s, $\mathrm{N\underline{H}CH_2}$)	13.6; 20.0; 32.5; 45.0; 94.9; 126.0 (2C); 128.8 (4C); 129.2 (2C); 131.2; 135.2; 135.4; 137.4; 164.4; 186.6	379
3k	0.97 (6H, d, J = 6.7, $\mathrm{CH(C\underline{H}_3)_2}$); 1.84 (1H, sept, J = 6.7, $\mathrm{C\underline{H}Me_2}$); 3.00 (2H, t, J = 6.3, $\mathrm{NHC\underline{H}_2}$); 5.34 (1H, s, =CH–CS); 6.86 (1H, dddd, J = 8.4, J = 8.3, J = 2.5, J = 0.8, H-4 ArF); 7.03 (1H, dd, J = 8.0, J = 1.7, H-6 ArF); 7.10 (1H, ddd, J = 10.1, J = 2.3, J = 2.2, H-2 ArF); 7.23 (2H, d, J = 8.5, H ArCl); 7.28 (1H, ddd, J = 8.6, J = 8.4, J = 6.5, H-5 ArF); 7.39 (2H, d, J = 8.5, H ArCl); 7.62 (1H, br. s, CSNH); 11.95 (1H, br. s, $\mathrm{N\underline{H}CH_2}$)	20.2 (2C); 29.4; 52.9; 95.3; 111.6 (d, ^2J = 23.9); 112.5 (d, ^2J = 21.2); 119.8 (d, ^4J = 1.8); 128.8 (2C); 128.9 (2C); 130.2 (d, ^3J = 9.3); 135.3; 135.4; 140.4 (d, ^3J = 10.0); 162.8 (d, ^1J = 246.6); 164.7; 186.4	363
3l	0.98 (3H, t, J = 7.4, $\mathrm{(CH_2)_2C\underline{H}_3}$); 1.61 (2H, sext, J = 7.3, $\mathrm{CH_2C\underline{H}_2Me}$); 3.14 (2H, dt, J = 7.0, J = 6.2, $\mathrm{NHC\underline{H}_2}$); 5.25 (1H, s, =CH–CS); 7.17 (1H, dd, J = 8.6, J = 2.5, H-6 $\mathrm{ArCl_2}$); 7.24 (2H, d, J = 8.4, H ArCl); 7.38 (1H, d, J = 8.7, H-5 $\mathrm{ArCl_2}$); 7.40 (2H, d, J = 8.4, H ArCl); 7.47 (1H, d, J = 2.4, H-2 $\mathrm{ArCl_2}$); 7.50 (1H, br. s, CSNH); 11.91 (1H, br. s, $\mathrm{N\underline{H}CH_2}$)	11.5; 23.8; 47.1; 95.6; 123.8; 126.1; 128.8 (2C); 128.9 (2C); 129.2; 130.6; 132.8; 135.1; 135.6; 138.3; 164.7; 186.5	399
3m	0.97 (3H, t, J = 7.4, $\mathrm{(CH_2)_2C\underline{H}_3}$); 1.60 (2H, sext, J = 7.3, $\mathrm{CH_2C\underline{H}_2Me}$); 2.31 (3H, s, $\mathrm{ArC\underline{H}_3}$); 3.08 (2H, dt, J = 6.9, J = 6.0, $\mathrm{NHC\underline{H}_2}$); 5.20 (1H, s, =CH–CS); 7.13 (4H, s, H Ar); 7.19 (2H, d, J = 4.5, H-3,5 Py); 7.78 (1H, br. s, CSNH); 8.65 (2H, d, J = 4.5, H-2,6 Py); 11.76 (1H, br. s, $\mathrm{N\underline{H}CH_2}$)	11.4; 21.0; 23.8; 46.9; 94.2; 122.1 (2C); 125.0 (2C); 129.8 (2C); 136.0; 136.2, 144.7; 150.1 (2C); 161.9; 187.6	312
3n	0.97 (3H, t, J = 7.4, $\mathrm{(CH_2)_2C\underline{H}_3}$); 1.59 (2H, sext, J = 7.3, $\mathrm{CH_2C\underline{H}_2Me}$); 3.07 (2H, dt, J = 6.7, J = 5.8, $\mathrm{NHC\underline{H}_2}$); 3.78 (3H, s, $\mathrm{OCH_3}$); 5.10 (1H, s, =CH–CS); 6.85 (2H, d, J = 8.9, H Ar); 7.16 (2H, d, J = 8.8, H Ar); 7.19 (2H, d, J = 5.6, H-3,5 Py); 7.72 (1H, br. s, CSNH); 8.65 (2H, d, J = 5.8, H-2,6 Py); 11.73 (1H, br. s, $\mathrm{N\underline{H}CH_2}$)	11.4; 23.8; 46.9; 55.4; 94.0; 114.4 (2C); 122.1 (2C); 127.0 (2C); 127.5; 131.5; 144.7; 150.1 (2C); 158.0; 188.0	328
3o	0.97 (3H, t, J = 7.4, $\mathrm{(CH_2)_2C\underline{H}_3}$); 1.59 (2H, sext, J = 7.3, $\mathrm{CH_2C\underline{H}_2Me}$); 2.94 (6H, s, $\mathrm{N(CH_3)_2}$); 3.06 (2H, dt, J = 6.9, J = 6.1, $\mathrm{NHC\underline{H}_2}$); 5.13 (1H, s, =CH–CS); 6.65 (2H, d, J = 8.8, H Ar); 7.08 (2H, d, J = 6.8, H Ar); 7.19 (2H, d, J = 5.4, H-3,5 Py); 7.71 (1H, br. s, CSNH); 8.64 (2H, d, J = 5.9, H-2,6 Py); 11.68 (1H, br. s, $\mathrm{N\underline{H}CH_2}$)	11.5; 23.9; 40.5 (2C); 46.9; 93.3; 112.4 (2C); 122.2 (2C); 126.6 (2C); 127.6; 144.9; 149.1; 150.1 (2C); 161.7; 187.8	341
3p	0.97 (3H, t, J = 7.4, $\mathrm{(CH_2)_2C\underline{H}_3}$); 1.61 (2H, sext, J = 7.2, $\mathrm{CH_2C\underline{H}_2Me}$); 3.10 (2H, dt, J = 6.9, J = 6.0, $\mathrm{NHC\underline{H}_2}$); 5.18 (1H, s, =CH–CS); 7.21 (2H, d, J = 6.0, H-3,5 Py); 7.23 (2H, d, J = 8.7, H Ar); 7.30 (2H, d, J = 8.7, H Ar); 7.70 (1H, br. s, CSNH); 8.68 (2H, d, J = 5.9, H-2,6 Py); 11.83 (1H, br. s, $\mathrm{N\underline{H}CH_2}$)	11.4; 23.8; 47.0; 94.7; 122.0 (2C); 126.1 (2C); 129.3 (2C); 131.4; 137.2; 144.5; 150.2 (2C); 162.2; 187.5	332
3q	0.98 (3H, t, J = 7.4, $\mathrm{(CH_2)_2C\underline{H}_3}$); 1.61 (2H, sext, J = 7.2, $\mathrm{CH_2C\underline{H}_2Me}$); 3.11 (2H, dt, J = 6.8, J = 6.1, $\mathrm{NHC\underline{H}_2}$); 5.27 (1H, s, =CH–CS); 6.88 (1H, dddd, J = 8.4, J = 8.3, J = 2.5, J = 0.7, H-4 Ar); 7.04 (1H, dd, J = 8.0, J = 1.8, H-6 Ar); 7.11 (1H, ddd, J = 10.0, J = 2.1, J = 2.0, H-2 Ar); 7.22 (2H, d, J = 6.0, H-3,5 Py); 7.28 (1H, ddd, J = 8.2, J = 8.1, J = 6.4, H-5 Ar); 7.75 (1H, br. s, CSNH); 8.69 (2H, d, J = 6.0, H-2,6 Py); 11.88 (1H, br. s, $\mathrm{N\underline{H}CH_2}$)	11.4; 23.8; 47.0; 95.0; 111.7 (d, ^2J = 23.5); 112.7 (d, ^2J = 20.2); 119.9; 122.0 (2C); 130.3 (d, ^3J = 7.9); 140.2 (d, ^3J = 8.8); 144.5; 150.2 (2C); 162.4; 162.8 (d, ^1J = 246.7); 187.4	316

TABLE 3 (continued)

1	2	3	4
3r	0.97 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.60 (2H, sext, J = 7.2, $CH_2C\underline{H}_2Me$); 3.10 (2H, dt, J = 6.9, J = 6.1, $NHC\underline{H}_2$); 5.19 (1H, s, =CH–CS); 7.19 (1H, dd, J = 8.6, J = 2.4, H-6 Ar); 7.22 (2H, d, J = 6.0, H-3,5 Py); 7.39 (1H, d, J = 8.6, H-5 Ar); 7.49 (1H, d, J = 2.4, H-2 Ar); 7.74 (1H, br. s, CSNH); 8.70 (2H, d, J = 5.9, H-2,6 Py); 11.85 (1H, br. s, $N\underline{H}CH_2$)	11.4; 23.8; 47.0; 95.4; 122.0 (2C); 123.8; 126.1; 129.3; 130.6; 132.7; 138.2; 144.4; 150.2 (2C); 162.3; 187.4	366
3s	0.98 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.62 (2H, sext, J = 7.2, $CH_2C\underline{H}_2Me$); 3.13 (2H, dt, J = 6.9, J = 6.1, $NHC\underline{H}_2$); 5.31 (1H, s, =CH–CS); 6.87 (1H, dddd, J = 8.4, J = 8.3, J = 2.5, J = 0.7, H-4 Ar); 7.06 (1H, dd, J = 8.2, J = 1.5, H-6 Ar); 7.11 (1H, ddd, J = 9.9, J = 2.1, J = 2.0, H-2 Ar); 7.28 (1H, ddd, J = 8.4, J =8.2, J = 6.3, H-5 Ar); 7.36 (1H, ddd, J = 7.8, J = 4.9, J = 0.9, H-5 Py); 7.63 (1H, ddd, J = 7.8, J = 2.3, J = 1.7, H-4 Py); 7.84 (1H, br. s, CSNH); 8.59 (1H, dd, J = 2.3, J = 0.9, H-2 Py); 8.66 (1H, dd, J = 4.9, J = 1.7, H-6 Py); 11.92 (1H, br. s, $N\underline{H}CH_2$)	11.4; 23.8; 47.0; 95.9; 111.6 (d, ^2J = 23.9); 112.6 (d, ^2J = 21.1); 119.9 (d, ^4J = 2.1); 123.3; 130.2 (d, ^3J = 8.9); 132.9; 135.1; 140.4 (d, ^3J = 10.0); 148.1; 150.4; 161.8; 162.8 (d, ^1J = 246.7); 187.1	316
3t	0.98 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.62 (2H, sext, J = 7.3, $CH_2C\underline{H}_2Me$); 2.32 (3H, s, $C_6H_4C\underline{H}_3$); 3.12 (2H, dt, J = 6.9, J = 6.0, $NHC\underline{H}_2$); 5.29 (1H, s, =CH–CS); 7.00 (1H, d, J = 7.7, H-4(6) Ar); 7.05-7.10 (2H, m, H-2,6(4) Ar); 7.21 (1H, dd, J = 7.7, J = 7.6, H-5 Ar); 7.33 (1H, ddd, J = 7.8, J = 4.9, J = 0.9, H-5 Py); 7.61 (1H, ddd, J = 7.8, J = 2.2, J = 1.8, H-4 Py); 7.74 (1H, br. s, CSNH); 8.57 (1H, dd, J = 2.2, J = 0.7, H-2 Py); 8.64 (1H, dd, J = 4.9, J = 1.7, H-6 Py); 11.83 (1H, br. s, $N\underline{H}CH_2$)	11.5; 21.3; 23.8; 47.0; 95.2; 122.0; 123.2; 125.4; 127.0; 129.0; 133.0; 135.1; 138.6; 139.2; 148.2; 150.3; 161.5; 187.2	312
3u	0.97 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.61 (2H, sext, J = 7.2, $CH_2C\underline{H}_2Me$); 3.10 (2H, dt, J = 6.9, J = 6.0, $NHC\underline{H}_2$); 3.78 (3H, s, OCH_3); 5.14 (1H, s, =CH–CS); 6.85 (2H, d, J = 8.8, H Ar); 7.17 (2H, d, J = 8.2, H Ar); 7.32 (1H, ddd, J = 7.8, J = 4.9, J = 0.8, H-5 Py); 7.59 (1H, ddd, J = 7.8, J = 2.0, J = 1.7, H-4 Py); 7.69 (1H, br. s, CSNH); 8.55 (1H, dd, J = 2.2, J = 0.9, H-2 Py); 8.63 (1H, dd, J = 4.8, J = 1.4, H-6 Py); 11.78 (1H, br. s, $N\underline{H}CH_2$)	11.5; 23.8; 46.9; 55.4; 94.8; 114.4 (2C); 123.2; 127.0 (2C); 131.6; 133.1; 135.1; 148.2; 150.3; 158.0; 161.3; 187.8	328
4a	0.84 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.62 (2H, sext, J = 7.3, $CH_2C\underline{H}_2Me$); 3.40 (2H, t, J = 7.3, NCH_2); 6.08 (1H, s, H-4); 7.05 (2H, d, J = 8.6, H-2,6 Ar); 7.32 (2H, d, J = 8.5, H-3,5 Ar); 7.42-7.46 (2H, m, H-2,6 Ph); 7.46-7.49 (2H, m, H-3,5 Ph); 7.48-7.50 (1H, m, H-4 Ph)	10.9 (CH_3); 22.8 ($\underline{C}H_2Me$); 52.8 (NCH_2); 108.0 (C-4); 121.8 (2C, C-2,6 ArCl); 128.2 (3C, C-2,6 Ph, C-4 ArCl); 128.9 (2C, C-3,5 Ph); 129.5 (2C, C-3,5 ArCl); 130.1 (C-4 Ph); 131.1 (C-1 Ph); 151.5 (C-1 ArCl); 163.7 (C-3); 167.4 (C-5)	329
4b	0.85 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.62 (2H, sext, J = 7.3, $CH_2C\underline{H}_2Me$); 3.42 (2H, t, J = 7.3, NCH_2); 6.09 (1H, s, H-4); 6.76 (1H, dddd, J = 8.4, J = 8.3, J = 2.5, J = 0.7, H-4 Ar); 6.84 (1H, ddd, J = 10.8, J = 2.1, J = 2.0, H-2 Ar); 6.90 (1H, ddd, J = 8.0, J = 1.9, J = 0.9, H-6 Ar); 7.31 (1H, ddd, J = 8.2, J = 8.1, J = 6.8, H-5 Ar); 7.42-7.46 (2H, m, H-2,6 Ph); 7.46-7.49 (2H, m, H-3,5 Ph); 7.48-7.50 (1H, m, H-4 Ph)	10.9 (CH_3); 22.8 ($\underline{C}H_2Me$); 52.7 (NCH_2); 107.5 (d, ^2J = 21.9, C-2 ArF); 108.0 (C-4); 110.1 (d, ^2J = 21.0, C-4 ArF); 116.1 (C-6 ArF); 128.3 (2C, C-2,6 Ph); 128.9 (2C, C-3,5 Ph); 130.1 (C-4 Ph); 130.5 (d, ^3J = 9.5, C-5 ArF); 131.0 (C-1 Ph); 154.7 (d, ^3J = 7.4, C-1 ArF); 163.7 (d, ^1J = 245.9, C-3 ArF); 163.7 (C-3); 167.6 (C-5)	313
4c	0.84 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.60 (2H, sext, J = 7.3, $CH_2C\underline{H}_2Me$); 2.34 (3H, s, $C_6H_4C\underline{H}_3$); 3.36 (2H, t, J = 7.4, NCH_2); 3.87 (3H, s, OCH_3); 6.05 (1H, s, H-4); 6.98 (2H, d, J = 8.8, H-3,5 ArOMe); 7.02 (2H, d, J = 8.3, H-2,6 ArMe); 7.17 (2H, d, J = 8.1, H-3,5 ArMe); 7.38 (2H, d, J = 8.8, H-2,6 ArOMe)	10.9 (CH_3); 20.9 ($Ar\underline{C}H_3$); 22.6 ($\underline{C}H_2Me$); 53.1 (NCH_2); 55.3 (OCH_3); 107.6 (C-4); 114.2 (2C, C-3,5 ArOMe); 120.2 (2C, C-2,6 ArMe); 123.6 (C-1 ArOMe); 129.6 (2C, C-2,6 ArOMe); 130.0 (2C, C-3,5 ArMe); 132.9 (C-4 ArMe); 150.6 (C-1 ArMe); 160.8 (C-4 ArOMe); 163.3 (C-3); 166.8 (C-5)	339
4d	0.84 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.59 (2H, sext, J = 7.4, $CH_2C\underline{H}_2Me$); 3.35 (2H, t, J = 7.3, NCH_2); 3.81 (3H, s, OCH_3); 3.86 (3H, s, OCH_3); 6.04 (1H, s, H-4); 6.91 (2H, d, J = 8.8, H-3,5 NAr); 6.98 (2H, d, J = 8.7, H-3,5 3-Ar); 7.05 (2H, d, J = 8.9, H-2,6 NAr); 7.38 (2H, d, J = 8.7, H-2,6 3-Ar)	10.9 (CH_3); 22.6 ($\underline{C}H_2Me$); 53.2 (NCH_2); 55.3 (OCH_3); 55.4 (OCH_3); 107.6 (C-4); 114.2 (2C, C-3,5 NAr); 114.6 (2C, C-3,5 3-Ar); 121.4 (2C, C-2,6 NAr); 123.6 (C-1 3-Ar); 129.6 (2C, C-2,6 3-Ar); 146.5 (C-1 NAr); 155.8 (C-4 NAr); 160.8 (C-4 3-Ar); 163.3 (C-3); 166.6 (C-5)	355

TABLE 3 (continued)

1	2	3	4
4e	0.84 (3H, t, *J* = 7.4, $(CH_2)_2C\underline{H}_3$); 1.60 (2H, sextet, *J* = 7.3, $CH_2C\underline{H}_2Me$); 3.37 (2H, t, *J* = 7.3, NCH_2); 3.87 (3H, s, OCH_3); 6.04 (1H, s, H-4); 6.99 (2H, d, *J* = 8.7, H-3,5 ArOMe); 7.03-7.06 (4H, m, H ArF); 7.38 (2H, d, *J* = 8.6, H-2,6 ArOMe)	10.9 (CH_3); 22.6 ($\underline{C}H_2Me$); 53.1 (NCH_2); 55.3 (OCH_3); 107.3 (C-4); 114.3 (2C, C-3,5 ArOMe); 116.0 (2C, d, ^{2}J = 22.3, C-3,5 ArF); 121.6 (2C, d, ^{3}J = 7.9, C-2,6 ArF); 123.4 (C-1 ArOMe); 129.6 (2C, C-2,6 ArOMe); 149.3 (d, ^{4}J = 1.9, C-1 ArF); 159.0 (d, ^{1}J = 242.0, C-4 ArF); 160.9 (C-4 ArOMe); 163.7 (C-3); 167.5 (C-5)	343
4f	0.84 (3H, t, *J* = 7.4, $(CH_2)_2C\underline{H}_3$); 1.61 (2H, sextet, *J* = 7.4, $CH_2C\underline{H}_2Me$); 3.41 (2H, t, *J* = 7.3, NCH_2); 3.86 (3H, s, OCH_3); 6.05 (1H, s, H-4); 6.74 (1H, dddd, *J* = 8.4, *J* = 8.3, *J* = 2.5, *J* = 0.7, H-4 ArF); 6.83 (1H, ddd, *J* = 10.8, *J* = 2.3, *J* = 2.2, H-2 ArF); 6.89 (1H, ddd, *J* = 8.0, *J* = 2.0, *J* = 0.8, H-6 ArF); 6.99 (2H, d, *J* = 8.8, H-2,6 ArOMe); 7.29 (1H, ddd, *J* = 8.0, *J* = 7.9, *J* = 6.7, H-5 ArF); 7.37 (2H, d, *J* = 8.8, H-3,5 ArOMe)	10.9 (CH_3); 22.8 ($\underline{C}H_2Me$); 52.9 (NCH_2); 55.4 (OCH_3); 107.5 (d, ^{2}J = 21.3, C-2 ArF); 107.5 (C-4); 110.0 (d, ^{2}J = 21.5, C-4 ArF); 114.3 (2C, C-3,5 ArOMe); 116.2 (C-6 ArF); 123.2 (C-1 ArOMe); 129.7 (2C, C-2,6 ArOMe); 130.5 (d, ^{3}J = 9.2, C-5 ArF); 154.7 (d, ^{3}J = 9.2, C-1 ArF); 161.0 (C-4 ArOMe); 163.6 (d, ^{1}J = 245.9, C-3 ArF); 163.7 (C-3); 167.7 (C-5)	343
4g	0.83 (3H, t, *J* = 7.4, $(CH_2)_3C\underline{H}_3$); 1.23 (2H, sextet, *J* = 7.4, $(CH_2)_2C\underline{H}_2Me$); 1.54 (2H, quintet, *J* = 7.5, $NCH_2C\underline{H}_2Et$); 3.37 (2H, t, *J* = 7.4, NCH_2); 6.10 (1H, s, H-4); 7.05-7.11 (1H, m, H-4 Ph); 7.07–7.13 (2H, m, H-2,6 Ph); 7.32-7.40 (2H, m, H-3,5 Ph); 7.38 (2H, d, *J* = 8.4, H-2,6 Ar); 7.46 (2H, d, *J* = 8.5, H-3,5 Ar)	13.6 ($CH_2\underline{C}H_3$); 19.6 ($\underline{C}H_2Me$); 31.3 ($NCH_2\underline{C}H_2$); 51.3 (NCH_2); 108.7 (C-4); 120.3 (2C, C-2,6 Ph); 123.7 (C-4 Ph); 129.2 (2C, C-3,5 Ar); 129.5 (4C, C-3,5 Ph, C-2,6 Ar); 129.7 (C-1 Ar); 136.1 (C-4 Ar); 152.9 (C-1 Ph); 162.1 (C-3); 166.7 (C-5)	343
4h	0.83 (3H, t, *J* = 7.4, $(CH_2)_3C\underline{H}_3$); 1.23 (2H, sextet, *J* = 7.4, $(CH_2)_2C\underline{H}_2Me$); 1.54 (2H, tt, *J* = 7.4, *J* = 6.0, $NCH_2C\underline{H}_2Et$); 2.35 (3H, s, $C_6H_4C\underline{H}_3$); 3.35 (2H, t, *J* = 7.3, NCH_2); 6.09 (1H, s, H-4); 7.01 (2H, d, *J* = 8.3, H-2,6 ArMe); 7.18 (2H, d, *J* = 8.3, H-3,5 ArMe); 7.39 (2H, d, *J* = 8.5, H-2,6 ArCl); 7.46 (2H, d, *J* = 8.5, H-3,5 ArCl)	13.6 ($CH_2\underline{C}H_3$); 19.6 ($\underline{C}H_2Me$); 21.0 ($Ar\underline{C}H_3$); 31.3 ($NCH_2\underline{C}H_2$); 51.4 (NCH_2); 108.8 (C-4); 120.1 (2C, C-2,6 ArMe); 129.2 (2C, C-3,5 ArCl); 129.5 (2C, C-3,5 ArMe); 129.8 (C-1 ArCl); 130.1 (2C, C-2,6 ArCl); 133.2 (C-4 ArMe); 136.1 (C-4 ArCl); 150.4 (C-1 ArMe); 162.0 (C-3); 166.4 (C-5)	357
4i	0.86 (6H, d, *J* = 6.7, $CH(C\underline{H}_3)_2$); 1.97 (1H, septet, *J* = 6.8, $C\underline{H}Me_2$); 3.15 (2H, d, *J* = 7.4, NCH_2); 3.81 (3H, s, OCH_3); 6.05 (1H, s, H-4); 6.91 (2H, d, *J* = 8.9, H-3,5 ArOMe); 7.05 (2H, d, *J* = 8.7, H-2,6 ArOMe); 7.36 (2H, d, *J* = 8.4, H-2,6 ArCl); 7.45 (2H, d, *J* = 8.4, H-3,5 ArCl)	19.8 (2C, $CH(\underline{C}H_3)_2$); 29.2 ($\underline{C}HMe_2$); 55.4 (OCH_3); 58.8 (NCH_2); 107.9 (C-4); 114.7 (2C, C-3,5 ArOMe); 121.3 (2C, C-2,6 ArOMe); 129.2 (2C, C-3,5 ArCl); 129.6 (2C, C-2,6 ArCl); 129.9 (C-1 ArCl); 136.0 (C-4 ArCl); 146.3 (C-1 ArOMe); 155.9 (C-4 ArOMe); 162.1 (C-3); 166.1 (C-5)	373
4j	0.84 (3H, t, *J* = 7.4, $(CH_2)_3C\underline{H}_3$); 1.24 (2H, sextet, *J* = 7.4, $(CH_2)_2C\underline{H}_2Me$); 1.55 (2H, quintet, *J* = 7.5, $NCH_2C\underline{H}_2Et$); 3.39 (2H, t, *J* = 7.3, NCH_2); 6.07 (1H, s, H-4); 7.03 (2H, d, *J* = 8.6, H-2,6 NAr); 7.32 (2H, d, *J* = 8.6 H-3,5 NAr); 7.38 (2H, d, *J* = 8.4, H-2,6 3-Ar); 7.47 (2H, d, *J* = 8.5, H-3,5 3-Ar)	13.6 ($CH_2\underline{C}H_3$); 19.6 ($\underline{C}H_2Me$); 31.4 ($NCH_2\underline{C}H_2$); 51.2 (NCH_2); 108.5 (C-4); 121.7 (2C, C-2,6 NAr); 128.4 (C-4 NAr); 129.2 (2C, C-2,6(3,5) 3-Ar); 129.5 (3C, C-1 3-Ar, C-3,5(2,6) 3-Ar); 129.5 (2C, C-3,5 NAr); 136.3 (C-4 3-Ar); 151.4 (C-1 NAr); 162.3 (C-3); 167.1 (C-5)	377
4k	0.86 (6H, d, *J* = 6.7, $CH(C\underline{H}_3)_2$); 1.98 (1H, septet, $C\underline{H}Me_2$); 3.21 (2H, d, *J* = 7.5, NCH_2); 6.05 (1H, s, H-4); 6.76 (1H, dddd, *J* = 8.5, *J* = 8.4, *J* = 2.4, *J* = 0.7, H-4 ArF); 6.82 (1H, ddd, *J* = 10.7, *J* = 2.2, *J* = 2.1, H-2 ArF); 6.89 (1H, ddd, *J* = 8.0, *J* = 1.9, *J* = 0.9, H-6 ArF); 7.30 (1H, ddd, *J* = 7.9, *J* = 7.8, *J* = 7.0, H-5 ArF); 7.37 (2H, d, *J* = 8.4, H-2,6 ArCl); 7.46 (2H, d, *J* = 8.5, H-3,5 ArCl)	19.8 (2C, $CH(\underline{C}H_3)_2$); 29.3 ($\underline{C}HMe_2$); 58.4 (NCH_2); 107.4 (d, ^{2}J = 21.8, C-2 ArF); 107.8 (C-4); 110.2 (d, ^{2}J = 21.4, C-4 ArF); 116.1 (C-6 ArF); 129.2 (2C, C-3,5 ArCl); 129.6 (C-1 ArCl); 129.7 (2C, C-2,6 ArCl); 130.6 (d, ^{3}J = 9.7, C-5 ArF); 136.2 (C-4 ArCl); 154.6 (d, ^{3}J = 8.3, C-1 ArF); 162.4 (C-3); 163.7 (d, ^{1}J = 246.2, C-3 ArF); 167.2 (C-5)	361
4l	0.85 (3H, t, *J* = 7.4, $(CH_2)_2C\underline{H}_3$); 1.62 (2H, sextet, *J* = 7.3, $CH_2C\underline{H}_2Me$); 3.40 (2H, t, *J* = 7.3, NCH_2); 6.06 (1H, s, H-4); 6.94 (1H, dd, *J* = 8.6, *J* = 2.5, H-6 $ArCl_2$); 7.19 (1H, d, *J* = 2.5, H-2 $ArCl_2$); 7.38 (2H, d, *J* = 8.4, H-2,6 ArCl); 7.40 (1H, d, *J* = 8.4, H-5 $ArCl_2$); 7.47 (2H, d, *J* = 8.4, H-3,5 ArCl)	10.9 (CH_3); 22.8 ($\underline{C}H_2Me$); 52.8 (NCH_2); 108.4 (C-4); 120.3 (C-6 $ArCl_2$); 122.1 (C-2 $ArCl_2$); 126.3 (C-4 $ArCl_2$); 129.3 (C-1 ArCl); 129.3 (2C, C-3,5 ArCl); 129.5 (2C, C-2,6 ArCl); 131.0 (C-5 $ArCl_2$); 133.0 (C-3 $ArCl_2$); 136.4 (C-4 ArCl); 152.3 (C-1 $ArCl_2$); 162.6 (C-3); 167.7 (C-5)	397

TABLE 3 (continued)

1	2	3	4
4m	0.85 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.61 (2H, sext, J = 7.4, $CH_2C\underline{H}_2Me$); 2.35 (3H, s, $C_6H_4C\underline{H}_3$); 3.34 (2H, t, J = 7.3, NCH_2); 6.18 (1H, s, H-4); 7.00 (2H, d, J = 8.3, H-2,6 Ar); 7.19 (2H, d, J = 8.0, H-3,5 Ar); 7.36 (2H, d, J = 4.4, H-3,5 Py); 8.75 (2H, d, J = 4.5, H-2,6 Py)	10.9 (CH_3); 20.9 (Ar$\underline{C}H_3$); 22.6 ($\underline{C}H_2Me$); 53.2 (NCH_2); 109.9 (C-4); 120.0 (2C, C-2,6 Ar); 122.4 (2C, C-3,5 Py); 130.1 (2C, C-3,5 Ar); 133.5 (C-4 Ar); 139.0 (C-4 Py); 150.2 (C-1 Ar); 150.5 (2C, C-2,6 Py); 160.2 (C-3); 165.9 (C-5)	310
4n	0.86 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.62 (2H, sext, J = 7.3, $CH_2C\underline{H}_2Me$); 3.34 (2H, t, J = 7.3, NCH_2); 3.83 (3H, s, OCH_3); 6.18 (1H, s, H-4); 6.93 (2H, d, J = 8.9, H-3,5 Ar); 7.05 (2H, d, J = 8.9, H-2,6 Ar); 7.36 (2H, d, J = 6.0, H-3,5 Py); 8.75 (2H, d, J = 6.0, H-2,6 Py)	10.9 (CH_3); 22.5 ($\underline{C}H_2Me$); 53.3 (NCH_2); 55.4 (OCH_3); 110.0 (C-4); 114.7 (2C, C-3,5 Ar); 121.3 (2C, C-2,6 Ar); 122.4 (2C, C-3,5 Py); 139.0 (C-4 Py); 146.0 (C-1 Ar); 150.5 (2C, C-2,6 Py); 156.1 (C-4 Ar); 160.1 (C-3); 165.5 (C-5)	326
4o	0.86 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.62 (2H, sext, J = 7.4, $CH_2C\underline{H}_2Me$); 2.97 (6H, s, $N(CH_3)_2$); 3.32 (2H, t, J = 7.4, NCH_2); 6.21 (1H, s, H-4); 6.78 (2H, d, J = 9.0, H-3,5 Ar); 7.04 (2H, d, J = 9.0, H-2,6 Ar); 7.37 (2H, d, J = 6.0, H-3,5 Py); 8.74 (2H, d, J = 6.0, H-2,6 Py)	10.9 (CH_3); 22.5 ($\underline{C}H_2Me$); 40.8 (2C, $N(CH_3)_2$); 53.5 (NCH_2); 110.6 (C-4); 113.3 (2C, C-3,5 Ar); 121.2 (2C, C-2,6 Ar); 122.3 (2C, C-3,5 Py); 139.2 (C-4 Py); 142.3 (C-1 Ar); 147.5 (C-4 Ar); 150.5 (2C, C-2,6 Py); 159.5 (C-3); 163.8 (C-5)	339
4p	0.86 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.62 (2H, sext, J = 7.3, $CH_2C\underline{H}_2Me$); 3.37 (2H, t, J = 7.3, NCH_2); 6.16 (1H, s, H-4); 7.03 (2H, d, J = 8.6, H-2,6 Ar); 7.33 (2H, d, J = 8.6, H-3,5 Ar); 7.36 (2H, d, J = 5.9, H-3,5 Py); 8.76 (2H, d, J = 6.0, H-2,6 Py)	10.9 (CH_3); 22.7 ($\underline{C}H_2Me$); 53.0 (NCH_2); 109.6 (C-4); 121.6 (2C, C-2,6 Ar); 122.4 (2C, C-3,5 Py); 128.7 (C-4 Ar); 129.6 (2C, C-3,5 Ar); 138.7 (C-4 Py); 150.6 (2C, C-2,6 Py); 151.2 (C-1 Ar); 160.5 (C-3); 166.7 (C-5)	330
4q	0.86 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.63 (2H, sext, J = 7.3, $CH_2C\underline{H}_2Me$); 3.39 (2H, t, J = 7.3, NCH_2); 6.17 (1H, s, H-4); 6.79 (1H, dddd, J = 8.4, J = 8.4, J = 2.5, J = 0.8, H-4 Ar); 6.82 (1H, ddd, J = 10.5, J = 2.1, J = 2.0, H-2 Ar); 6.88 (1H, ddd, J = 8.0, J = 1.8, J = 0.7, H-6 Ar); 7.32 (1H, ddd, J = 8.0, J = 7.9, J = 6.7, H-5 Ar); 7.36 (2H, d, J = 6.0, H-3,5 Py); 8.77 (2H, d, J = 6.0, H-2,6 Py)	10.8 (CH_3); 22.7 ($\underline{C}H_2Me$); 52.9 (NCH_2); 107.4 (d, ^2J = 21.9, C-2 Ar); 109.5 (C-4); 110.5 (d, ^2J = 21.5, C-4 Ar); 115.9 (d, ^4J = 2.1, C-6 Ar); 122.4 (2C, C-3,5 Py); 130.6 (d, ^3J = 9.6, C-5 Ar); 138.7 (C-4 Py); 150.6 (2C, C-2,6 Py); 154.3 (d, ^3J = 8.9, C-1 Ar); 160.5 (C-3); 163.6 (d, ^1J = 246.3, C-3 Ar); 167.0 (C-5)	314
4r	0.86 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.63 (2H, sext, J = 7.4, $CH_2C\underline{H}_2Me$); 3.41 (2H, t, J = 7.3, NCH_2); 6.15 (1H, s, H-4); 6.94 (1H, dd, J = 8.6, J = 2.4, H-6 Ar); 7.19 (1H, d, J = 2.4, H-2 Ar); 7.35 (2H, d, J = 5.9, H-3,5 Py); 7.41 (1H, d, J = 8.6, H-5 Ar); 8.77 (2H, d, J = 5.9, H-2,6 Py)	10.8 (CH_3); 22.8 ($\underline{C}H_2Me$); 52.9 (NCH_2); 109.4 (C-4); 120.1 (C-6 Ar); 122.0 (C-2 Ar); 122.4 (2C, C-3,5 Py); 126.6 (C-4 Ar); 131.1 (C-5 Ar); 133.0 (C-3 Ar); 138.5 (C-4 Py); 150.6 (2C, C-2,6 Py); 152.1 (C-1 Ar); 160.7 (C-3); 167.3 (C-5)	364
4s	0.86 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.63 (2H, sext, J = 7.4, $CH_2C\underline{H}_2Me$); 3.39 (2H, t, J = 7.3, NCH_2); 6.13 (1H, s, H-4); 6.78 (1H, dddd, J = 8.5, J = 8.4, J = 2.4, J = 1.3, H-4 Ar); 6.82 (2H, ddd, J = 10.8, J = 2.0, J = 2.0, H-2 Ar); 6.89 (1H, ddd, J = 7.7, J = 1.2, J = 0.7, H-6 Ar); 7.31 (1H, ddd, J = 7.9, J = 7.8, J = 7.0, H-5 Ar); 7.44 (1H, ddd, J = 7.9, J = 4.9, J = 0.7, H-5 Py); 7.77 (1H, ddd, J = 7.8, J = 1.9, J = 1.7, H-4 Py); 8.72-8.75 (2H, m, H-2,6 Py)	10.9 (CH_3); 22.8 ($\underline{C}H_2Me$); 52.9 (NCH_2); 107.4 (d, ^2J = 21.9, C-2 Ar); 109.1 (C-4); 110.5 (d, ^2J = 21.3, C-4 Ar); 116.0 (C-6 Ar); 123.7 (C-5 Py); 127.2 (C-3 Py); 130.6 (d, ^3J = 9.6, C-5 Ar); 135.6 (C-4 Py); 148.9 (C-2 Py); 151.2 (C-6 Py);154.5 (d, ^3J = 8.2, C-1 Ar); 159.9 (C-3); 163.7 (d, ^1J = 246.2, C-3 Ar); 167.1 (C-5)	314
4t	0.85 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.61 (2H, sext, J = 7.3, $CH_2C\underline{H}_2Me$); 2.37 (3H, s, $C_6H_4C\underline{H}_3$); 3.34 (2H, t, J = 7.3, NCH_2); 6.14 (1H, s, H-4); 6.89-6.93 (2H, m, H-4,6 Ar); 6.93 (1H, d, J = 0.5, H-2 Ar); 7.27 (1H, dd, J = 7.4, J = 7.3, H-5 Ar); 7.43 (1H, ddd, J = 7.9, J = 4.9, J = 0.9, H-5 Py); 7.77 (1H, ddd, J = 7.9, J = 2.2, J = 1.8, H-4 Py); 8.72 (1H, dd, J = 4.9, J = 1.7, H-6 Py); 8.73 (1H, dd, J = 2.3, J = 0.8, H-2 Py)	10.9 (CH_3); 21.6 (Ar$\underline{C}H_3$); 22.7 ($\underline{C}H_2Me$); 53.0 (NCH_2); 109.3 (C-4); 116.9 (C-6 Ar); 121.1 (C-4 Ar); 123.7 (C-5 Py); 124.8 (C-2 Ar); 127.5 (C-3 Py); 129.4 (C-5 Ar); 135.6 (C-4 Py); 139.4 (C-3 Ar); 148.9 (C-2 Py); 151.0 (C-6 Py); 152.9 (C-1 Ar); 159.7 (C-3); 166.4 (C-5)	310
4u	0.83 (3H, t, J = 7.4, $(CH_2)_2C\underline{H}_3$); 1.61 (2H, sext, J = 7.4, $CH_2C\underline{H}_2Me$); 3.32 (2H, t, J = 7.3, NCH_2); 3.80 (3H, s, OCH_3); 6.12 (1H, s, H-4); 6.91 (2H, d, J = 9.0, H-3,5 Ar); 7.04 (2H, d, J = 9.0, H-2,6 Ar); 7.41 (1H, ddd, J = 7.9, J = 4.9, J = 0.8, H-5 Py); 7.75 (1H, ddd, J = 7.9, J = 2.2, J = 1.8, H-4 Py); 8.70 (1H, dd, J = 4.9, J = 1.7, H-6 Py); 8.72 (1H, dd, J = 2.3, J = 0.9, H-2 Py)	11.0 (CH_3); 22.7 ($\underline{C}H_2Me$); 53.3 (NCH_2); 55.6 (OCH_3); 109.5 (C-4); 114.8 (2C, C-3,5 Ar); 121.4 (2C, C-2,6 Ar); 123.8 (C-5 Py); 127.7 (C-3 Py); 135.7 (C-4 Py); 146.3 (C-1 Ar); 149.0 (C-2 Py); 151.1 (C-6 Py); 156.2 (C-4 Ar); 159.6 (C-3); 166.0 (C-5)	326

TABLE 3 (continued)

1	2	3	4
5d	0.88 (6H, d, J = 6.7, $\mathrm{CH(C\underline{H}_3)_2}$); 1.89 (1H, sept, J = 6.7, $\mathrm{C\underline{H}Me_2}$); 3.44 (2H, t, J = 6.7, $\mathrm{NHC\underline{H}_2}$); 3.83 (3H, s, $\mathrm{OCH_3}$); 5.84 (1H, br. s, $\mathrm{N\underline{H}CH_2}$); 6.95 (2H, d, J = 8.9, H Ar); 7.15 (2H, d, J = 9.0, H Ar); 7.56 (1H, br. s, $\mathrm{N\underline{H}Ar}$)	20.1 (2C); 28.0; 52.7; 55.5; 115.3 (2C); 127.7 (2C); 128.4; 158.9; 181.2	238
5h	0.91 (6H, d, J = 6.7, $\mathrm{CH(C\underline{H}_3)_2}$); 1.92 (1H, sept, J = 6.7, $\mathrm{C\underline{H}Me_2}$); 3.45 (2H, t, J = 6.0, $\mathrm{NHC\underline{H}_2}$); 6.21 (1H, br. s, $\mathrm{N\underline{H}CH_2}$); 6.93-7.05 (3H, m, H Ar); 7.28 (1H, ddd, J = 7.7, J = 7.5, J = 6.4, H-5 Ar); 8.60 (1H, br. s, $\mathrm{N\underline{H}Ar}$);	20.1 (2C); 27.9; 52.8; 112.0 (d, ^2J = 23.4); 113.8 (d, ^2J = 20.9); 120.2 (d, ^4J = 1.8); 131.3 (d, ^3J = 8.8); 137.9 (d, ^3J = 8.0); 163.3 (d, ^1J = 249.2); 180.2	227
6k	0.39 (1.5H, d, J = 6.7) and 0.47 (1.5H, d, J = 6.7, $\mathrm{CH(C\underline{H}_3)_2}$); 1.51-1.65 (1H, m, $\mathrm{C\underline{H}Me_2}$); 1.69 (3H, s, $\mathrm{CH_3}$); 3.13 (1H, dd, J =13.7, J = 6.4) and 3.98 (1H, dd, J = 13.7, J = 6.8, $\mathrm{NCH_2}$); 5.56 (1H, s, H-5); 6.54 (1H, ddd, J = 10.3, J = 2.3, J = 2.2, H-2 ArF); 6.59 (1H, ddd, J = 7.9, J = 1.8, J = 0.8, H-6 ArF); 6.80 (1H, dddd, J = 8.4, J = 8.5, J = 2.5, J = 0.8, H-4 ArF); 7.26 (1H, ddd, J = 8.4, J = 8.2, J = 6.3, H-5 ArF); 7.29 (2H, d, J = 8.6, H-2,6 ArCl); 7.33 (2H, d, J = 8.4, H-2,6 ArCl*); 7.41 (2H, d, J = 8.6, H-3,5 ArCl*); 7.48 (2H, d, J = 8.6, H-3,5 ArCl)	19.9 (0.5C) and 20.0 (0.5C, $\mathrm{CH(\underline{C}H_3)_2}$); 28.4 ($\mathrm{\underline{C}HMe_2}$); 30.6; 47.6; 54.1 ($\mathrm{NCH_2}$); 109.1 (d, ^2J = 21.9, C-2(4) ArF); 109.9 (d, ^2J = 21.3, C-4(2) ArF); 117.3; 117.8 (d, ^4J = 2.7, C-6 ArF); 127.9 (2C); 128.4 (2C); 128.7 (2C); 129.6 (2C); 129.6 (d, ^3J = 8.2, C-5 ArF); 133.2; 134.6; 135.4; 143.2; 144.3; 152.2 (d, ^3J = 9.7, C-1 ArF); 152.7; 163.1 (d, ^1J = 245.6, C-3 ArF)	499
7i	0.91 (6H, d, J =6.7, $\mathrm{CH(C\underline{H}_3)_2}$); 1.78 (1H, sept, J =6.5, $\mathrm{C\underline{H}Me_2}$); 2.94 (2H, t, J = 5.8, $\mathrm{NHC\underline{H}_2}$); 3.74 (3H, s, $\mathrm{OCH_3}$); 3.84 (3H, s, $\mathrm{OCH_3}$); 6.55 (2H, d, J = 8.6, ArOMe); 6.75 (2H, d, J = 8.7, ArOMe); 6.94 (2H, d, J = 8.8, ArOMe); 7.05 (2H, d, J = 8.7, ArOMe); 7.27 (2H, d, J = 8.0, ArCl); 7.39 (2H, d, J = 8.4, ArCl); 12.84 (1H, s, NH)	20.0 (2C); 29.2; 52.2; 55.4; 55.5; 97.1; 114.2 (2C); 114.5 (2C); 121.2 (2C); 122.7 (2C); 128.6 (2C); 129.2 (2C); 132.0; 134.5; 143.1; 144.8; 156.1; 156.9; 160.8; 163.2; 168.1	538
7k	0.92 (6H, d, J = 6.7, $\mathrm{CH(C\underline{H}_3)_2}$); 1.80 (1H, sept, J = 6.6, $\mathrm{C\underline{H}Me_2}$); 2.97 (2H, t, J = 6.1, $\mathrm{NHC\underline{H}_2}$); 6.31 (1H, d, J = 10.3, H-2 ArF); 6.38 (1H, d, J = 8.0, H-6 ArF); 6.68 (1H, ddd, J = 8.4, J = 8.4, J = 2.1, H-4 ArF); 6.84 (1H, d, J = 10.1, H-2 ArF*); 6.89 (1H, ddd, J = 8.8, J = 8.6, J = 2.1, H-4 ArF*); 6.91 (1H, d, J = 8.4, H-6 ArF*); 7.14 (1H, ddd, J = 8.0, J = 7.9, J = 6.5, H-5 ArF); 7.26 (2H, d, J = 8.3, H-2,6 ArCl); 7.35 (1H, ddd, J = 8.0, J = 8.0, J = 6.4, H-5 ArF*); 7.42 (2H, d, J = 8.5, H-3,5 ArCl); 12.77 (1H, s, NH)	20.0 (2C, $\mathrm{CH(\underline{C}H_3)_2}$); 29.1 ($\mathrm{\underline{C}HMe_2}$); 52.3 ($\mathrm{NCH_2}$); 97.1 (C-3); 107.4 (d, ^2J = 22.1, C-2 ArF); 109.1 (d, ^2J = 22.4, C-2 ArF*); 110.3 (d, ^2J = 21.5, C-4 ArF); 111.6 (d, ^2J = 21.1, C-4 ArF*); 115.7 (C-6 ArF); 117.4 (C-6 ArF*); 128.7 (2C, C-3,5 ArCl); 129.0 (2C, C-2,6 ArCl); 130.1 (d, ^3J = 9.6, C-5 ArF); 130.6 (d, ^3J = 9.3, C-5 ArF*); 131.5 (C-1 ArCl); 134.9 (C-4 ArCl); 151.1 (d, ^3J = 9.2, C-1 ArF*); 152.6 (d, ^3J = 8.9, C-1 ArF); 161.7 (C-2(4)); 163.2 (d, ^1J = 245.7, C-3 ArF); 163.4 (d, ^1J = 247.1, C-3 ArF*); 164.1 ($\mathrm{C{=}\underline{C}NH}$); 168.6 (C-4(2))	514
8i	3.78 (3H, s, $\mathrm{OCH_3}$); 3.85 (3H, s, $\mathrm{OCH_3}$); 6.76 (2H, d, J = 8.9, H ArOMe); 6.84 (2H, d, J = 8.9, H ArOMe); 6.97 (2H, d, J = 8.9, H ArOMe); 7.33 (2H, d, J = 8.8, H ArOMe); 7.34 (2H, d, J = 8.5, H ArCl); 7.72 (2H, d, J = 8.5, H ArCl); 11.82 (1H, s, OH)	55.4; 55.6; 104.8; 114.6 (2C); 114.9 (2C); 121.1 (2C); 126.8 (2C); 127.8 (2C); 130.2 (3C); 136.9; 138.1; 144.9; 156.8; 159.4; 162.2; 175.5; 191.3	483
8n	3.77 (3H, s, $\mathrm{OCH_3}$); 3.86 (3H, s, $\mathrm{OCH_3}$); 6.71 (2H, d, J = 8.8, H Ar); 6.81 (2H, d, J = 8.9, H Ar); 6.99 (2H, d, J = 8.9, H Ar); 7.34 (2H, d, J = 8.9, H Ar); 7.49 (2H, d, J = 6.0, H-3,5 Py); 8.66 (2H, d, J = 6.0, H-2,6 Py); 12.08 (1H, s, OH)	55.4; 55.6; 104.7; 114.6 (2C); 115.0 (2C); 121.1 (2C); 121.7 (2C); 126.8 (2C); 130.0; 144.2; 147.6; 149.3 (2C); 156.8; 159.6; 160.7; 176.5; 190.5	450

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*The signals of the second aryl fragment.

water, electrospray ionization, positive ion current recording. Elemental analysis was performed on an EA 1106 equipment (Carlo Erba Instruments). Melting points were recorded on a Kofler bench. The purity of the obtained compounds was controlled by TLC on 60Å F_{254} silica gel plates (Merck). The reagents and solvents were purchased from Acros and Alfa Aesar and were used without additional purification.

Preparation of *N*-Alkylimines of Acetophenones and Acetylpyridines (Intermediates A) (General Method). The interaction of the ketones **1a-e** with primary amines in the presence of $TiCl_4$ required 48 h according to the literature method [21]. After the reaction was complete, the mixture was filtered through Celite and the solvent was removed by evaporation at reduced pressure. The imines that formed were further isolated according to the method [26]. The obtained product contained ~90% of the target imine and up to 10% of the starting acetophenone (according to the ^{1}H NMR spectrum and LC/MS), and could be used in the next stage without additional purification.

4-Methoxyacetophenone *N*-Propylimine. Light-yellow oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.04 (3H, t, $J = 6.6$, $CH_2C\underline{H}_3$); 1.97 (2H, sext, $J = 6.2$, $CH_2C\underline{H}_2Me$); 2.79 (3H, s, $N{=}CCH_3$); 3.10-3.24 (1H, m) and 3.60-3.74 (1H, m, NCH_2); 3.90 (3H, s, OCH_3); 7.10 (2H, d, $J = 7.2$, H Ar); 8.20 (2H, d, $J = 7.3$, H Ar). Mass spectrum, *m*/*z* (I_{rel}, %): 192 $[M+H]^+$ (100).

***N*-(4-Chlorophenyl)amide of (*Z*)-3-Phenyl-3-propylaminoprop-2-enethioic Acid (3a)**. A mixture of acetophenone *N*-propylimine (7.74 g, 48 mmol) and 4-chlorophenylisothiocyanate (8.25 g, 49 mmol) in anhydrous MeCN (10 ml) was stirred for 72 h at room temperature, and the crystalline precipitate **3a** was filtered off, recrystallized from MTBE, and air-dried. Yield 11.59 g (73%).

The thioamides **3b-u** were obtained similarly.

The mother liquors obtained after collecting the crystalline compound **3n** were evaporated and separated by silica gel chromatography (elution with a petroleum ether–CH_2Cl_2 system, gradient from 1:1 to 1:10, with added Et_3N (0.5%)). The product was **3,5-bis(4-methoxyphenylimino)-4-(4-pyridoyl)-1,2-di-thiolane (8n)**. Yield 0.4 g (6%).

Reaction of 3-Fluorophenylisothiocyanate with 4-Chloroacetophenone *N*-Isobutylimine. A mixture of 4-chloroacetophenone *N*-isobutylimine (6.62 g, 31.6 mmol) obtained by the method [20] and 3-fluorophenylisothiocyanate (4.37 g, 28.5 mmol) in anhydrous Et_2O (10 ml) was stirred at room temperature for 72 h, then the crystalline precipitate of compound **3k** was filtered off. Yield 2.97 g, 29%. The filtrate was evaporated and separated by chromatography on silica gel (eluting with petroleum ether–Et_2O, gradient from 10:0 to 5:2, with added Et_3N (0.5%)). The elution sequence was: compound **7k** (0.31 g, 4%), 4-chloroacetophenone (1.4 g, 29%), compound **6k** (1.12 g, 14%), an additional crop of compound **3k** (0.58 g), for a total yield of 3.55 g, 34%, and the thiourea **5h** (1.48 g, 23%).

Similarly, the reaction of 4-chloroacetophenone *N*-isobutylimine (6.15 g, 29.3 mmol) with 4-methoxyphenylisothiocyanate (4.63 g, 28.0 mmol), followed by silica gel column chromatography (elution with petroleum ether MTBE, gradient from 10:0 to 5:2, with added Et_3N (0.5%)) yielded the target thioamide **3i** (4.84 g, 46%), the thiourea **5d** (1.33 g, 20%), and also the 1,2-dithiolanes **7i** (0.10 g, 1%) and **8i** (0.17 g, 3%).

5-(4-Chlorophenylimino)-3-phenyl-2-propyl-2,5-dihydroisothiazole (4a). Pyridine (2.9 ml, 37 mmol) was added to a solution of the thioanilide **3a** (11.58 g, 35 mmol) in anhydrous $CHCl_3$ (35.0 ml). The reaction mixture was cooled to 0-5°C, followed by a dropwise addition of iodine solution (8.88 g, 35 mmol) in EtOH (60.0 ml) over 3 h and stirring at the same temperature for another 1 h. After the reaction was complete, the solvent was evaporated, the residue was treated with Et_2O (50 ml), the precipitated crystals were filtered off, redissolved in $CHCl_3$ (40 ml), extracted with saturated aqueous Na_2CO_3 (60 ml) and H_2O (60 ml), the solvent was removed at reduced pressure, the residue was recrystallized from MTBE and air-dried.

Compounds **4b-u** were obtained by an analogous method.

The X-ray structural analysis of compounds **3k**, **4p**, **4r**, **6k**, **7k**, **8n** was performed on a Nonius KappaCDD automated diffractometer to $2\theta_{max}$ 55° (λ(Mo) 0.71073 Å). Compound **3k** ($C_{19}H_{20}FClN_2S$) formed monoclinic crystals, at 293 K: *a* 9.7096(6), *b* 19.7188(14), *c* 10.3650(8) Å; β 108.648(4)°; *V* 1880.3(2) Å^3; space group $P2_1/n$; *Z* 4; d_{calc} 1.278 g/cm^3; μ 0.326 mm^{-1}; *F*(000) 756. Compound **4p** ($C_{17}H_{16}N_3ClS$) formed triclinic crystals, at 173 K: *a* 6.7490(3), *b* 9.6460(3), *c* 13.4060(7) Å; α 95.996(1), β 98.8560(1), γ 107.861(1)°; *V* 810.15(4) Å^3; space group $P\bar{1}$; Z 2; d_{calc} 1.352 g/cm^3; μ 0.364 mm^{-1}; *F*(000) 344. Compound **4r** ($C_{17}H_{15}N_3Cl_2S$) formed triclinic crystals, at 173 K: *a* 6.8560(2), *b* 9.6910(3), *c* 13.2340(5) Å; α 95.975(2), β 93.839(2), γ 108.382(2)°; *V* 825.24(5) Å^3; space group $P\bar{1}$; *Z* 2; d_{calc} 1.466 g/cm^3; μ 0.521 mm^{-1}; *F*(000) 376. Compound **6k** ($C_{27}H_{25}Cl_2FN_2S$) formed monoclinic crystals, at 293 K: *a* 10.7328(3), *b* 23.6570(9), *c* 11.0874 (4) Å; β 155.219(3)°; *V* 2546.8(1) Å^3; space group $P2_1$; *Z* 4; d_{calc} 1.303 g/cm^3; μ 0.363 mm^{-1}; *F*(000) 1040. Compound **7k** ($C_{26}H_{22}ClF_2N_3S_2$) formed triclinic crystals, at 190 K: *a* 11.1036(3), *b* 12.0797(3), *c* 19.9825(7) Å; α 99.112(1), β 103.434(1), γ 106.634(2)°; *V* 2423.98(12) Å^3; space group $P\bar{1}$; *Z* 4 (*Z'* 2); d_{calc} 1.409 g/cm^3, μ 0.366 mm^{-1}; *F*(000) 1064. Compound **8n** ($C_{23}H_{19}N_3O_3S_2$) formed monoclinic crystals, at 183 K: *a* 13.9793(6), *b* 7.3442(2), *c* 19.6917(12) Å; β 90.5430(10)°; *V* 2021.59(16) Å^3; space group $P2_1/c$; *Z* 4; d_{calc} 1.477 g/cm^3; μ 0.296 mm^{-1}; *F*(000) 936.

The unit cell parameters and the intensities of 7132 reflections for compound **3k**, 5687 reflections (3669 independent, R_{int} 0.0176) for compound **4p**, 5692 reflections (3749 independent, R_{int} 0.0308) for compound **4r**, 9764 reflections for compound **6k**, 15878 reflections (10923 independent, R_{int} 0.040) for compound **7k**, 7826 reflections (4248 independent, R_{int} 0.1007) for compound **8n** were measured on a Bruker-Nonius KappaCCD automated X-ray diffractometer (λMoKα radiation, λ 0.71073 Å, graphite monochromator). The structures of the compounds were solved by the direct method with SIR2004 software [30] and were refined with SHELXL software package [31] in anisotropic approximation for non-hydrogen atoms. The hydrogen atom positions were calculated geometrically, taking into account the differential synthesis of electron density and were refined with the "rider" model at $U_{\text{iso}} = 1.5U_{\text{eq}}$ for the methyl group and $U_{\text{iso}} = 1.2U_{\text{eq}}$ for the rest of the hydrogen atoms. The final probability factors for the structures **3k**, **4p**, **4r**, **6k**, **7k**, and **8n** were respectively R_1 0.0785, wR_2 0.1965; R_1 0.0373, wR_2 0.0919; R_1 0.0459, wR_2 0.1154; R_1 0.0817, wR_2 0.2429; R_1 0.095, wR_2 0.301; and R_1 0.0581, wR_2 0.0993. The complete crystallographic data sets for compounds **3k**, **4p**, **4r**, **6k**, **7k**, and **8n** were deposited at the Cambridge Crystallographic Data Center (deposits CCDC 976565, CCDC 956666, CCDC 956665, CCDC 976566, CCDC 979541, and CCDC 957328, respectively).

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