Reaction of 3-aryl-2-cyanothioacrylamides with dimethyl acetylenecarboxylate, methyl propiolate, and *N*-phenylmaleimide

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The reaction of cyanothioacrylamides with dimethyl acetylenedicarboxylate, methyl propiolate, and *N*-phenylmaleimide was studied. The reaction follows a cycloaddition pathway to give thiopyrans, irrespective of the electronic or spatial effects of the substituents in the thioamide group and in position 3 of the 1-thiabuta-1,3-diene system. The reaction is regio- and stereoselective.

Key words: cyanothioacrylamides, cycloaddition, dimethyl acetylenedicarboxylate, methylpropiolate, *N*-phenylmaleimide, thiopyrans.

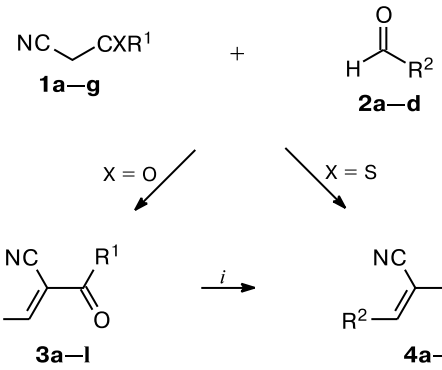
The reaction of thioamides with acetylenes has long attracted keen attention of chemists.[1—8] This is due, first of all, to the diversity of possible reaction routes. The structures of the reactants and the reaction conditions have a pronounced effect on the reaction outcome. The electronic effects of substituents, both proximate to and remote from the thioamide fragment,[1—3] and the use of catalysts and solvents are also important factors. Some thioamides are able to undergo [4π+2π]-cycloaddition both as dienes (due to the electron-deficient C=S bond[4]) and as dienophiles.[5] It was shown[6,7] that the thioamide group can be incorporated in the 1-thiabuta-1,3-diene fragment of a thioacrylamide and, in this case, the amide is involved in the Diels—Alder reaction as a diene but only after pre-activation by acylation. Cyanothioacrylamides react with dimethyl acetylenedicarboxylate and methyl propiolate to give aryl-4*H*-thiopyrancarbonitriles without preliminary acylation.[8]

The purpose of this work was to study the effect of the structural fragments in the thiocarbamoyl group and the substituent in position 3 on the reactivity of cyanothioacrylamides toward cycloaddition with acetylenes and olefins.

The reaction of cyanoacetamides **1a—g** with aromatic aldehydes **2a—d** gave 3-aryl-2-cyanoacrylamides **3a—l**. By treatment with the Lawesson´s reagent, compounds **3a—k** were converted into 3-aryl-2-cyanoacrylthioamides **4a—k**, containing different substituents at the nitrogen atom of the thioamide group and in the aromatic ring (Scheme 1, Table 1). *N*-Unsubstituted thioamide **4l** was obtained by the reaction of cyanothioacetamide with thiophene-2-carbaldehyde (**2d**).

In principle, the reaction of 2-cyanoacrylthioamides **4** with alkyl acetylenedicarboxylates can proceed by several routes, which may yield either cycloaddition products, or the products of addition at the triple bond, or cyclocondensation products.

Scheme 1



1: R^1 = NH_2 (**a**), NHMe (**b**), *cyclo*-C_5H_9NH (**c**), *cyclo*-$C_6H_{11}NH$ (**d**), *cyclo*-$C_7H_{13}NH$ (**e**), N⟨ ⟩ (**f**), N⟨ ⟩N–C$_6$H$_4$–OMe (**g**)
2: R^2 = 4-ClC_6H_4 (**a**), 4-MeC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**), 2-thienyl (**d**)
3, 4: R^2 = 4-ClC_6H_4, R^1 = NHMe (**a**), *cyclo*-C_5H_9NH (**b**), *cyclo*-$C_6H_{11}NH$ (**c**), *cyclo*-$C_7H_{13}NH$ (**d**), N⟨ ⟩ (**e**);
R^2 = 4-MeC_6H_4, R^1 = NHMe (**f**), *cyclo*-$C_6H_{11}NH$ (**g**);
R^2 =  , R^1 = *cyclo*-$C_6H_{11}NH$ (**h**), N⟨ ⟩N–C$_6$H$_4$–OMe (**i**);
R^2 = 4-$MeOC_6H_4$, R^1 = NHMe (**j**), *cyclo*-$C_6H_{11}NH$ (**k**); R^2 = 2-thienyl, R^1 = NH_2 (**l**)

i. Lawesson´s reagent.

The reactions of 2-cyanothioacrylamides **4** with dienophiles were carried out under various conditions (room temperature or refluxing in solvents) using various solvents (dichloromethane, benzene, toluene, xylene) and

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Table 1. Yields, melting points, and elemental analysis data of 3-aryl-2-cyanoacrylamides **3** and 3-aryl-2-cyanothioacrylamides **4**

Compound	Procedure	Yield (%)	M.p. /°C	Found / Calculated (%), N	Molecular formula
3-(4-Chlorophenyl)-2-cyano-*N*-methylacrylamide (**3a**)	*A*	75	157—159	12.06 / 11.84	$C_{11}H_9ClN_2O$
3-(4-Chlorophenyl)-2-cyano-*N*-cyclopentylacrylamide (**3b**)	*A*	83	161—162	10.31 / 10.20	$C_{15}H_{15}ClN_2O$
3-(4-Chlorophenyl)-2-cyano-*N*-cyclohexylacrylamide (**3c**)	*B*	70	160—161	9.82 / 9.70	$C_{16}H_{17}ClN_2O$
3-(4-Chlorophenyl)-2-cyano-*N*-cycloheptylacrylamide (**3d**)	*A*	83	123—125	9.25 / 9.20	$C_{17}H_{17}ClN_2O$
3-(4-Chlorophenyl)-2-(pyrrolidinocarbonyl)acrylonitrile (**3e**)	*A*	90	83—85	10.75 / 10.70	$C_{14}H_{13}ClN_2O$
2-Cyano-*N*-methyl-3-(*p*-tolyl)acrylamide (**3f**)	*A*	72	136—138	13.80 / 13.99	$C_{12}H_{12}N_2$
2-Cyano-*N*-cyclohexyl-3-(*p*-tolyl)acrylamide (**3g**)	*B*	86	125—127	10.20 / 10.44	$C_{17}H_{20}N_2O$
3-Benzo[1,3]dioxol-5-yl-2-cyano-*N*-cyclohexylacrylamide (**3h**)	*B*	88	169—170	9.48 / 9.40	$C_{17}H_{18}N_2O_3$
3-Benzo[1,3]dioxol-5-yl-2-[4-(4-methoxyphenyl)-piperazino-1-ylcarbonyl]acrylonitrile (**3i**)	*A*	53	163—164	10.67 / 10.27	$C_{22}H_{21}N_3O_4$
2-Cyano-3-(4-methoxyphenyl)-*N*-methylacrylamide (**3j**)	*A*	79	145—147	12.80 / 12.95	$C_{12}H_{12}N_2O_2$
2-Cyano-*N*-cyclohexyl-3-(4-methoxyphenyl)-acrylamide (**3k**)	*B*	65	138—139	9.70 / 9.85	$C_{17}H_{20}N_2O_2$
2-Cyano-3-thiophen-2-ylacrylamide (**3l**)	*B*	62	168—170	12.51 / 12.58	$C_{10}H_7ClN_2S$
3-(4-Chlorophenyl)-2-cyano-*N*-methylthioacrylamide (**4a**)	*C*	75	156—158	12.06 / 11.84	$C_{11}H_9ClN_2S$
3-(4-Chlorophenyl)-2-cyano-*N*-cyclopentylthioacrylamide (**4b**)	*C*	43	129—131	10.02 / 9.64	$C_{15}H_{15}ClN_2S$
3-(4-Chlorophenyl)-2-cyano-*N*-cyclohexylthioacrylamide (**4c**)	*C*	66	158—160	9.34 / 9.20	$C_{16}H_{17}ClN_2S$
3-(4-Chlorophenyl)-2-cyano-*N*-cycloheptylthioacrylamide (**4d**)	*C*	70	88—90	8.94 / 8.73	$C_{17}H_{19}ClN_2S$
3-(4-Chlorophenyl)-2-(pyrrolidinocarbothioyl)-acrylonitrile (**4e**)	*C*	45	158—160	9.34 / 9.20	$C_{14}H_{13}ClN_2S$
2-Cyano-*N*-methyl-3-(*p*-tolyl)thioacrylamide (**4f**)	*C*	81	142—144	12.80 / 12.95	$C_{12}H_{12}N_2S$
2-Cyano-*N*-cyclohexyl-3-(*p*-tolyl)thioacrylamide (**4g**)	*C*	65	137—138	9.65 / 9.85	$C_{17}H_{20}N_2S$
3-Benzo[1,3]dioxol-5-yl-2-(cyclohexylaminocarbothioyl)acrylonitrile (**4h**)	*C*	93	161—163	8.57 / 8.92	$C_{17}H_{18}N_2O_2S$
3-Benzo[1,3]dioxol-5-yl-2-[4-(4-methoxyphenyl)-piperazino-1-ylcarbonylthio]acrylonitrile (**4i**)	*C*	87	127—129	10.40 / 10.32	$C_{22}H_{21}N_3O_3S$
2-Cyano-3-(4-methoxyphenyl)-*N*-methylthioacrylamide (**4j**)	*C*	60	129—131	12.00 / 12.06	$C_{12}H_{12}N_2OS$
2-Cyano-*N*-cyclohexyl-3-(4-methoxyphenyl)-thioacrylamide (**4k**)	*C*	72	154—156	9.46 / 9.32	$C_{17}H_{20}N_2OS$
2-Cyano-3-(thiophen-2-yl)thioacrylamide (**4l**)	*D*	80	141—142	14.30 / 14.42	$C_8H_6N_2S_2$

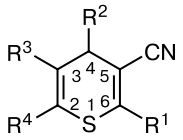
reactant ratios. The formation of products was detected even at room temperature, but in this case, the process was very slow; even after 1—3 months the reaction mixture still contained substantial amounts of the reactants. The conditions of choice are refluxing in an inert solvent (xylene, toluene, benzene) using a three- to five-fold excess of dienophile.

On the basis of the IR, mass, and ^1H and ^{13}C NMR spectra (Table 2—4), and elemental analysis data (see Table 1), it was found that the reactions of 2-cyanoacryl-

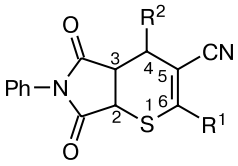
Table 2. Yields, melting points, and mass spectrometry and elemental analysis data for 6-amino-4-aryl(hetaryl)-5-cyano-4*H*-thiopyrans **5—9** and hexahydrothiopyrano[2,3-*c*]pyrrolecarbonitrile derivatives **10**

Compound	Yield (%)	M.p. /°C	Found / Calculated (%)			Molecular formula	Mass spectrum, *m/z* (*I* (%))
			C	H	N		
Dimethyl 6-amino-4-(4-chlorophenyl)-5-cyano-4*H*-thiopyran-2,3-dicarboxylate (**5a**)	46	98—100	52.59 52.68	3.41 3.59	7.82 7.68	$C_{16}H_{13}ClN_2O_4S$	364 (12.6)
Methyl 6-amino-4-(4-chlorophenyl)-5-cyano-4*H*-thiopyran-3-carboxylate (**5b**)	63	200—201	54.78 54.81	3.55 3.61	9.72 9.84	$C_{14}H_{11}ClN_2O_2S$	306 (25.8)
Dimethyl 4-(4-chlorophenyl)-5-cyano-6-cyclohexylamino-4*H*-thiopyran-2,3-dicarboxylate (**5c**)	61	118—120	59.06 59.12	5.02 5.19	6.05 6.27	$C_{22}H_{23}ClN_2O_4S$	446 (17.4)
Methyl 4-(4-chlorophenyl)-5-cyano-6-cyclohexylamino-4*H*-thiopyran-3-carboxylate (**5d**)	45	90—91	61.79 61.77	5.33 5.44	7.35 7.21	$C_{20}H_{21}ClN_2O_2S$	388 (44.7)
Dimethyl 4-(4-chlorophenyl)-5-cyano-6-cyclopentylamino-4*H*-thiopyran-2,3-dicarboxylate (**5e**)	54	111—112	58.22 58.26	4.80 4.89	6.08 6.47	$C_{21}H_{21}ClN_2O_4S$	432 (23.9)
Dimethyl 4-(4-chlorophenyl)-5-cyano-6-cycloheptylamino-4*H*-thiopyran-2,3-dicarboxylate (**5f**)	45	109—110	59.89 59.93	5.39 5.47	5.59 6.05	$C_{23}H_{25}ClN_2O_4S$	462 (13.9)
Dimethyl 4-(4-chlorophenyl)-5-cyano-6-methylamino-4*H*-thiopyran-2,3-dicarboxylate (**5g**)	83	123—124	53.97 53.99	3.84 3.99	7.13 7.40	$C_{17}H_{15}ClN_2O_4S$	378 (12.3)
Methyl 4-(4-chlorophenyl)-5-cyano-6-methylamino-4*H*-thiopyran-3-carboxylate (**5h**)	35	118—120	56.13 56.16	4.01 4.08	8.90 8.74	$C_{15}H_{13}ClN_2O_2S$	320 (25.0)
Dimethyl 4-(4-chlorophenyl)-5-cyano-6-piperazine-4*H*-thiopyran-2,3-dicarboxylate (**5i**)	52	148—150	57.30 57.35	4.49 4.57	6.88 6.70	$C_{20}H_{19}ClN_2O_4S$	418 (18.7)
Dimethyl 5-cyano-6-cyclohexylamino-4-(*p*-tolyl)-4*H*-thiopyran-2,3-dicarboxylate (**6a**)	73	141—143	64.71 64.77	6.10 6.14	6.40 6.57	$C_{23}H_{26}N_2O_4S$	426 (12.2)
Methyl 5-cyano-6-cyclohexylamino-4-(*p*-tolyl)-4*H*-thiopyran-3-carboxylate (**6b**)	36	136—137	68.44 68.45	6.51 6.56	7.72 7.60	$C_{21}H_{24}N_2O_2S$	368 (35.0)
Dimethyl 5-cyano-6-methylamino-4-(*p*-tolyl)-4*H*-thiopyran-2,3-dicarboxylate (**6c**)	57	151—153	60.33 60.32	4.99 5.06	7.75 7.82	$C_{18}H_{18}N_2O_4S$	358 (11.2)
Methyl 5-cyano-6-methylamino-4-(*p*-tolyl)-4*H*-thiopyran-3-carboxylate (**6d**)	53	145—146	63.95 63.98	5.33 5.37	9.20 9.26	$C_{16}H_{18}N_2O_2S$	300 (32.2)
Dimethyl 4-(4-methoxyphenyl)-5-cyano-6-methylamino-4*H*-thiopyran-2,3-dicarboxylate (**7a**)	67	136—138	57.71 57.74	4.80 4.85	7.40 7.48	$C_{18}H_{18}N_2O_5S$	374 (5.3)
Methyl 4-(4-methoxyphenyl)-5-cyano-6-methylamino-4*H*-thiopyran-3-carboxylate (**7b**)	51	125—126	60.75 60.74	5.07 5.10	8.71 8.85	$C_{16}H_{16}N_2O_3S$	316 (56.7)
Dimethyl 4-(4-methoxyphenyl)-5-cyano-6-cyclohexylamino-4*H*-thiopyran-2,3-dicarboxylate (**7c**)	58	113—114	62.40 62.43	5.89 5.92	6.51 6.33	$C_{23}H_{26}N_2O_5S$	442 (42.1)
Dimethyl 4-benzo[1,3]dioxol-5-yl-5-cyano-6-[4-(4-methoxyphenyl)piperazino]-4*H*-thiopyran-2,3-dicarboxylate (**8a**)	52	123—124	61.15 61.19	4.91 4.95	5.94 6.14	$C_{28}H_{27}N_3O_7S$	549 (12.3)
Dimethyl 4-benzo[1,3]dioxol-5-yl-5-cyano-6-cyclohexylamino-4*H*-thiopyran-2,3-dicarboxylate (**8b**)	66	119—120	60.45 60.51	5.39 5.30	6.06 6.14	$C_{23}H_{24}ClN_2O_6S$	456 (13.1)
Methyl 6-amino-5-cyano-4-thiophen-2-yl-4*H*-thiopyran-3-carboxylate (**9**)	55	213—215	51.77 51.78	3.60 3.62	10.71 10.84	$C_{12}H_{10}N_2O_2S_2$	278 (41.9)
4-(4-Chlorophenyl)-2-cyclohexylamino-5,7-dioxo-6-phenyl-4,4a,5,6,7,7a-hexahydrothiopyrano[2,3-*c*]pyrrol-3-carbonitrile (**10a**)	60	229—231	65.36 65.33	5.01 5.06	8.88 8.79	$C_{26}H_{23}ClN_3O_2S$	477 (9.5)
4-(4-Methoxyphenyl)-2-methylamino-5,7-dioxo-6-phenyl-4,4a,5,6,7,7a-hexahydrothiopyrano[2,3-*c*]pyrrole-3-carbonitrile (**10b**)	56	167—169	65.12 65.17	4.70 4.72	10.21 10.36	$C_{22}H_{19}N_3O_3S$	405 (15.1)
4-Benzo[1,3]dioxol-5-yl-2-[4-(4-methoxyphenyl)-piperazin-1-yl]-5,7-dioxo-6-phenyl-4,4a,5,6,7,7a-hexahydrothiopyrano[2,3-*c*]pyrrole-3-carbonitrile (**10c**)	58	190—192	66.18 66.19	4.88 4.86	9.74 9.65	$C_{27}H_{24}N_3O_4S$	580 (2.4)
2-Amino-5,7-dioxo-6-phenyl-4-thiophen-2-yl-4,4a,5,6,7,7a-hexahydrothiopyrano[2,3-*c*]pyrrole-3-carbonitrile (**10d**)	62	155—157	58.80 58.84	3.50 3.57	9.63 9.95	$C_{18}H_{13}N_3O_2S_2$	367 (2.4)

Table 3. Spectroscopic characteristics of 6-amino-4-aryl(hetaryl)-5-cyano-4*H*-thiopyrans **5—9** and hexahydrothiopyrano[2,3-*c*]pyrrolecarbonitrile derivatives **10** *



5—9



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Compound	IR spectrum, ν/cm^{-1}				^{1}H NMR (DMSO-d$_6$), δ (*J*/Hz)			
	CH	NH	C≡N	C=O	R^1	R^2	C(4)H	R^3, R^4
5a	2950, 2930	3450	2190	1720, 1740	7.20 (s, 2 H, NH_2)	7.44, 7.27 (4 H, Ar, AA´BB´ system, *J* = 8.8)	4.71 (s)	3.66, 3.79 (both s, 3 H each, OMe)
5b	2950	3450	2180	1730, 1740	6.97 (s, 2 H, NH_2)	7.39, 7.24 (4 H, Ar, AA´BB´ system, *J* = 8.5)	4.59 (s)	3.64 (s, 3 H, OMe); 7.80 (s, 1 H, C(3)H)
5c	2930, 2850	3430	2190	1720, 1740	1.32—1.05, 1.90—1.51 (both m, 5 H each, CH_2, Cy); 3.79—3.58 (m, 1 H, CH, Cy); 7.29 (s, 1 H, NH)	7.43, 7.27 (4 H, Ar, AA´BB´ system, *J* = 8.5)	4.76 (s)	3.71, 3.79 (both s, 3 H each, OMe)
5d	3010, 2930	3450	2180	1710	1.33—1.05, 1.88—1.54 (both m, 5 H each, CH_2, Cy); 3.51—3.49 (m, 1 H, CH, Cy); 6.92 (d, 1 H, NH, *J* = 8.3)	7.40, 7.24 (4 H, Ar, AA´BB´ system, *J* = 8.5)	4.64 (s)	3.67 (s, 3 H, OMe); 7.83 (s, 1 H, C(3)H)
5e	2860, 2960	3450	2190	1730, 1740	1.71—1.57 (m, 6 H, CH_2, Cy); 1.92—1.88 (m, 2 H, CH_2, Cy); 4.11—4.08 (m, 1 H, CH, Cy); 7.14 (d, 1 H, NH, *J* = 7.3)	7.30, 7.24 (4 H, Ar, AA´BB´ system, *J* = 8.5)	4.69 (s)	3.73, 3.80 (both s, 3 H each, OMe)
5f	2930, 2850	3450	2190	1730, 1740	0.91—0.84 (m, 3 H, CH_2, Cy); 1.27—1.21 (m, 8 H, CH_2, Cy); 1.53—1.1.49 (m, 1 H, CH_2, Cy); 6.82 (d, 1 H, NH, *J* = 7.4)	7.31, 7.23 (4 H, Ar, AA´BB´ system, *J* = 8.5)	4.68 (s)	3.72, 3.81 (both s, 3 H each, OMe)
5g	2950, 2930	3450	2180	1680, 1720	2.96 (d, 3 H, Me, *J* = 4.9); 7.30 (d, 1 H, NH, *J* = 8.4)	7.30, 7.22 (4 H, Ar, AA´BB´ system, *J* = 8.6)	4.69 (s)	3.71, 3.80 (both s, 3 H each, OMe)
5h	2950	3450	2180	1720, 1740	2.92 (d, 3 H, Me, *J* = 4.9); 6.99 (q, 1 H, NH, *J* = 5.3)	7.28, 7.23 (4 H, Ar, AA´BB´ system, *J* = 8.9)	4.64 (s)	3.69 (s, 3 H, OMe); 7.68 (s, 1 H, C(3)H)
5i	2940, 2920	—	2190	1720, 1740	2.06—1.87 (m, 4 H, CH_2, Pyr); 3.53—3.49, 3.73—3.66 (both m, 2 H each, CH_2, Pyr)	7.31, 7.24 (4 H, Ar, AA´BB´ system, *J* = 8.2)	4.77 (s)	3.76, 3.81 (both s, 3 H each, OMe)
6a	2930, 2950	3290	2190	1720, 1750	1.25—1.80 (m, 10 H, CH_2); 3.60—3.41 (m, 1 H, CH); 6.78 (d, 1 H, NH, *J* = 8.6); 7.61 (s, 1 H, CH)	2.30 (s, 3 H, Me); 7.10 (s, 4 H, Ar)	4.61 (s)	3.70, 3.80 (both s, 3 H each, OMe)
6b	2940, 3090	3370	2180	1720	1.21—1.88 (m, 10 H, CH, Cy); 3.38—3.53 (m, 1 H, CH, Cy); 6.37 (d, 1 H, NH, *J* = 8.1)	2.29 (s, 3 H, Me); 7.05, 7.11 (4 H, Ar, AA´BB´ system, *J* = 8.4)	4.59 (s)	3.68 (s, 3 H, OMe); 7.61 (s, 1 H, C(3)H)

(*to be continued*)

Table 3 (*continued*)

Compound	IR spectrum, ν/cm^{-1}				^{1}H NMR (DMSO-d$_6$), δ (*J*/Hz)			
	CH	NH	C≡N	C=O	R^1	R^2	C(4)H	R^3, R^4
6c	2930, 2960	3330	2190	1720, 1740	2.95 (d, 3 H, Me, *J* = 4.9); 7.14 (d, 1 H, NH, *J* = 4.8)	2.30 (s, 3 H, Me); 7.09 (s, 4 H, Ar)	4.62 (s)	3.69, 3.80 (both s, 3 H each, OMe)
6d	2960, 3060	3300	2190	1720	2.91 (d, 3 H, Me, *J* = 4.9); 7.05 (q, 1 H, NH, *J* = 0.02)	2.29 (s, 3 H, Me); 7.05, 7.11 (4 H, Ar, AA´BB´ system, *J* = 8.2)	4.59 (s)	3.68 (s, 3 H, OMe); 7.63 (s, 1 H, C(3)H)
7a	2930, 2960, 2990	3320	2180	1730, 1750	2.95 (d, 3 H, Me, *J* = 4.88); 7.15 (q, 1 H, NH, *J* = 0.2)	3.79 (s, 3 H, OMe); 6.83, 7.14 (4 H, Ar, AA´BB´ system, *J* = 8.6)	4.60 (s)	3.69, 3.75 (both s, 3 H each, OMe)
7b	2930, 2950, 3000	3310	2190	1720	2.92 (d, 3 H, Me, *J* = 4.7); 6.86 (d, 1 H, NH, *J* = 4.7)	3.73 (s, 3 H, OMe); 6.78, 7.13 (4 H, Ar, AA´BB´ system, *J* = 8.4)	4.58 (s)	3.68 (s, 3 H, OMe); 7.60 (s, 1 H, C(3)H)
7c	2930, 2950, 2990	3320	2190	1720, 1740	1.20—1.23, 1.53—1.91 (both m, 5 H each, CH, Cy); 3.51—3.61 (m, 1 H, CH, Cy); 7.15 (s, 1 H, NH)	3.78 (s, 3 H, OMe); 6.91, 7.16 (4 H, Ar, AA´BB´ system, *J* = 8.6)	4.64 (s)	3.69, 3.73 (both s, 3 H each, OMe)
8a	2850, 2930	3400	2180	1710, 1740	3.16—3.03 (m, 4 H, CH_2); 3.54—3.47, 3.71—3.64 (both m, 2 H each, CH_2); 3.80 (s, 3 H, OMe); 6.84, 6.92 (4 H, Ar, AA´BB´ system, *J* = 9.4)	6.02 (s, 2 H, CH_2); 6.74 (dd, 1 H, CH, Ar, J_1 = 8.1, J_2 = 1.6); 6.80 (d, 1 H, CH, Ar, *J* = 1.6); 6.89 (d, 1 H, CH, Ar, *J* = 8.1)	4.80 (s)	3.68, 3.74 (both s, 3 H each, OMe)
8b	2840, 2920	3420	2180	1710, 1740	1.33—1.07 (m, 5 H, CH_2); 1.55 (d, 1 H, CH, *J* = 12.0); 1.72—1.66, 1.89—1.77 (both m, 2 H each, CH_2); 3.59—3.52 (m, 1 H, CH); 6.76 (d, 1 H, Ar, *J* = 1.8); 7.30, 7.24 (4 H, Ar, AA´BB´ system, *J* = 8.5)	6.01 (s, 2 H, CH_2); 6.71 (dd, 1 H, Ar, J_1 = 2.4, J_2 = 1.8); 6.88 (d, 1 H, Ar, *J* = 8.0); 7.16 (d, 1 H, NH, *J* = 8.2)	4.63 (s)	3.79, 3.81 (both s, 3 H each, OMe)
9	2950, 3080	3240, 3330, 3400	2200	1700	6.77 (s, 2 H, NH_2)	6.93—6.83 (m, 2 H, CH, Ar); 7.21 (dd, 1 H, CH, Ar, J_1 = 5.0, J_2 = 1.5)	4.93 (s)	3.73 (s, 3 H, OMe); 7.59 (s, 1 H, C(3)H)
10a	—	3440	2180	1700, 1680	1.31—1.06 (m, 10 H, CH); 3.67—3.59 (m, 1 H, CH); 7.18 (d, 1 H, NH, *J* = 8.3)	7.74, 7.51 (4 H, Ar, AA´BB´ system, *J* = 8.6)	4.09 (d, *J* = 3.8)	4.18 (dd, 1 H, CH, J_1 = 9.2, J_2 = 3.8); 4.86 (d, 1 H, CH, *J* = 9.2); 7.08—7.05 (m, 2 H, Ar); 7.44 (t, 1 H, Ar, *J* = 7.3); 7.51 (t, 2 H, Ar, *J* = 7.3)
10b	2930, 2990	3380	2180	1720, 1730	2.90 (d, 3 H, Me); 7.31 (s, 1 H, NH)	3.76 (s, 3 H, OMe); 6.93, 7.31 (4 H, Ar, AA´BB´ system, *J* = 8.7)	4.22 (d, *J* = 2.6)	4.71 (d, 1 H, CH, *J* = 9.4); 4.26 (dd, 1 H, CH, J_1 = 9.4; J_2 = 2.8); 7.21—7.26 (m, 2 H, CH, Ar); 7.48 (t, 1 H, Ar, *J* = 7.4); 7.56 (t, 1 H, Ar, *J* = 6.9)

(*to be continued*)

Table 3 (*continued*)

Compound	IR spectrum, ν/cm^{-1}				^{1}H NMR (DMSO-d$_6$), δ (*J*/Hz)			
	CH	NH	C≡N	C=O	R^1	R^2	C(4)H	R^3, R^4
10c	—	—	2180	1720, 1680	3.11—3.00 (m, 4 H, CH_2); 3.54—3.50 (m, 2 H, CH_2); 3.69 (s, 3 H, OMe); 3.77—3.73 (m, 2 H, CH_2); 6.93, 6.83 (4 H, Ar, AA´BB´ system, *J* = 9.2)	6.02 (s, 2 H, CH_2); 6.91 (d, 1 H, Ar, *J* = 8.8); 7.07 (dd, 1 H, Ar, J_1 = 8.8, J_2 = 1.6); 7.20 (d, 1 H, Ar, *J* = 1.6)	4.13 (d, *J* = 3.9)	4.93 (d, 1 H, CH, *J* = 8.7); 4.23 (dd, 1 H, CH, J_1 = 8.7, J_2 = 3.9); 7.11—7.15 (m, 2 H, CH, Ar); 7.44 (t, 1 H, Ar, *J* = 4.9); 7.51 (t, 1 H, Ar, *J* = 7.2)
10d	2920	3410	2190	1720, 1730	7.08 (s, 2 H, NH_2)	6.97 (dd, 1 H, Ar, J_1 = 5.1, J_2 = 3.4); 7.04 (d, 1 H, CH, Ar, *J* = 3.4); 7.39—7.42 (m, 1 H, Ar)	4.44 (d, *J* = 5.5)	3.91 (dd, 1 H, CH, J_1 = 9.9, J_2 = 5.5); 5.03 (d, 1 H, CH, *J* = 9); 6.83 (d, 2 H, CH, Ar, J_1 = 7.3); 7.46—7.38 (m, 3 H, Ar)

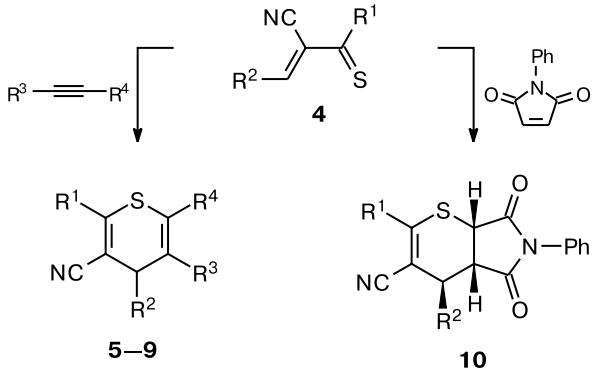
* The following designations are used: Cy is cycloalkyl, Pyr pyrrolidino.

Table 4. Spectroscopic characteristics of 3-aryl-2-cyanothioacrylamides **4**

Compound	Mass spectrum, *m/z* (*I* (%))	^{1}H NMR (DMSO-d$_6$), δ (*J*/Hz)		
		CH (s)	R^1	R^2
4a	236 (85.3)	7.97	3.11 (d, 3 H, Me, J_1 = 4.6); 10.58 (d, 1 H, NH, *J* = 4.6)	7.65, 7.93 (4 H, Ar, AA´BB´ system, *J* = 8.6)
4b	290 (100.0)	8.06	1.52—1.96 (m, 8 H, CH); 4.10—4.20 (m, 1 H, CH); 10.31—10.45 (m, 1 H, NH)	7.53, 7.92 (4 H, Ar, AA´BB´ system, *J* = 8.6)
4c	304 (100.0)	7.52	1.10—1.44 (m, 5 H, CH); 1.59—1.66 (m, 1 H, CH); 1.73—1.80, 1.94—2.01 (both m, 2 H each, CH); 4.17—4.27 (m, 1 H, CH); 10.37—10.42 (m, 1 H, NH)	7.65, 7.93 (4 H, Ar, AA´BB´ system, *J* = 8.6)
4d	320 (84.2)	7.89	0.87—0.92 (m, 3 H, CH); 1.18—1.32 (m, 9 H, CH); 1.63—1.69 (m, 2 H, CH); 3.57—3.66 (m, 1 H, CH); 10.22—10.29 (m, 1 H, NH)	7.53, 7.90 (4 H, Ar, AA´BB´ system, *J* = 8.6)
4e	276 (100.0)	7.60	1.82—2.07 (m, 4 H, CH); 3.07—3.46, 3.74—3.90 (both m, 2 H each, CH)	7.49, 7.88 (4 H, Ar, AA´BB´ system, *J* = 8.6)
4f	216 (100.0)	8.04	3.14 (d, 3 H, Me, *J* = 4.6); 10.08—10.22 (m, 1 H, NH)	2.41 (s, 3 H, Me); 7.32, 7.83 (4 H, Ar, AA´BB´ system, *J* = 8.6)
4g	284 (49.7)	8.02	1.13—1.45, 1.58—1.89 (both m, 5 H each, CH); 3.61—3.78 (m, 1 H, CH); 7.71—7.78 (m, 1 H, NH)	2.41 (s, 3 H, Me); 7.31, 7.82 (4 H, Ar, AA´BB´ system, *J* = 8.6)
4h	314 (87.8)	7.51	1.10—1.48 (m, 5 H, CH); 1.54—1.62 (m, 1 H, CH); 1.64—1.80, 1.89—2.02 (both m, 2 H each, CH); 4.15—4.25 (m, 1 H, CH); 10.16 (d, 1 H, NH, *J* = 7.5)	6.14 (s, 2 H, CH_2); 7.20 (d, 1 H, CH, Ar, *J* = 8.6); 7.52 (dd, 1 H, CH, Ar, J_1 = 8.8, J_2 = 1.4); 7.66 (d, 1 H, CH, Ar, *J* = 1.6)
4i	314 (56.2)	7.46	3.14—3.26 (m, 4 H, CH); 4.00—4.09, 4.29—4.37 (both m, 2 H each, CH); 3.69 (s, 3 H, OMe); 6.95, 6.52 (4 H, Ar, AA´BB´ system, *J* = 9.2)	6.16 (s, 2 H, CH_2); 7.11 (d, 1 H, CH, Ar, *J* = 8.7); 7.43 (dd, 1 H, CH, Ar, J_1 = 8.7, J_2 = 1.7); 7.56 (d, 1 H, CH, Ar, *J* = 1.7)
4j	232 (100.0)	8.07	3.14 (d, 3 H, Me, J_1 = 4.6); 9.99—10.08 (m, 1 H, NH)	3.87 (s, 3 H, OMe); 7.05, 7.94 (4 H, Ar, AA´BB´ system, *J* = 8.6)
4k	300 (52.3)	7.74	1.08—1.44 (m, 5 H, CH); 1.56—1.66 (m, 1 H, CH); 1.68—1.81, 1.90—2.01 (both m, 2 H each, CH); 4.18—4.30 (m, 1 H, CH); 10.20 (d, 1 H, NH, *J* = 7.5)	3.86 (s, 3 H, OMe); 7.13, 7.95 (4 H, Ar, AA´BB´ system, *J* = 9.2)
4l	194 (100.0)	8.41	9.18, 9.79 (both s, 1 H each, NH)	7.26 (dd, 1 H, CH, Ar, J_1 = 5.0, J_2 = 3.6); 7.85 (d, 1 H, CH, Ar, *J* = 3.6); 7.99 (d, 1 H, CH, Ar, *J* = 5.0)

thioamides **4** with alkyl acetylenecarboxylates yield only cycloaddition products **5—9**. No cyclocondensation products are formed (Scheme 2).

Scheme 2

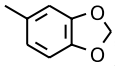
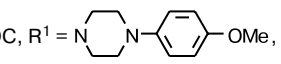


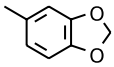
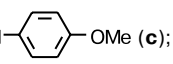
5—9 **10**

5: R^2 = 4-ClC_6H_4, R^3 = MeOOC, R^1 = NH_2, R^4 = MeOOC (**a**), H (**b**);
R^1 = *cyclo*-$C_6H_{11}NH$, R^4 = MeOOC (**c**), H (**d**);
R^1 = *cyclo*-C_5H_9NH, R^4 = MeOOC (**e**); R^1 = *cyclo*-$C_7H_{13}NH$,
R^4 = MeOOC (**f**); R^1 = NHMe, R^4 = MeOOC (**g**), H (**h**);

R^1 =  , R^4 = MeOOC (**i**)

6: R^2 = 4-MeC_6H_4, R^3 = MeOOC, R^1 = *cyclo*-$C_6H_{11}NH$,
R^4 = MeOOC (**a**), H (**b**); R^1 = NHMe, R^4 = MeOOC (**c**), H (**d**)
7: R^2 = 4-$MeOC_6H_4$, R^3 = MeOOC, R^1 = NHMe, R^4 = MeOOC (**a**),
H (**b**); R^1 = *cyclo*-$C_6H_{11}NH$, R^4 = MeOOC (**c**)

8: R^2 =  , R^3 = MeOOC, R^1 =  ,
R^4 = MeOOC (**a**); R^1 = *cyclo*-$C_6H_{11}NH$, R^4 = MeOOC (**b**)
9: R^2 = 2-thienyl, R^3 = MeOOC, R^1 = NH_2, R^4 = H
10: R^2 = 4-ClC_6H_4, R^1 = *cyclo*-$C_6H_{11}NH$ (**a**);
R^2 = 4-$MeOC_6H_4$, R^1 = NHMe (**b**);

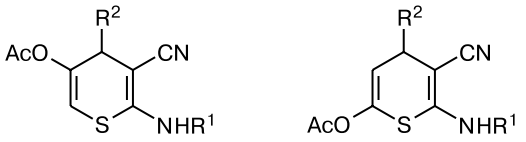
R^2 =  , R^1 =  (**c**);
R^2 = 2-thienyl, R^1 = NH_2 (**d**)

The ^{1}H NMR spectra of compounds **5—9** (see Table 3) exhibit two singlets (or one singlet for compounds with R^4 = H) due to the methoxycarbonyl groups in positions 2 and 3 of the thiopyran ring. The singlet for the C(4) proton shifts upfield compared to that for the starting compounds, in particular, to δ 4.58—4.93. This is due to the change in the hybridization of the carbon atom from sp^2 in cyanothioacrylamides **4** to sp^3 in 4*H*-thiopyrans **5—9**. In addition, the spectra contain signals for the aromatic protons and amino-group protons. The ^{13}C NMR spectrum fully confirms the formation of the 4*H*-thiopyran structure (Table 5).

The IR spectra of compounds **5—9** exhibit an absorption band at 3290—3450 cm^{-1} corresponding to the NH stretching vibrations, an absorption band at 2180—2200 cm^{-1} due to the CN vibrations, and strong bands at 1710—1730 cm^{-1}, typical of C=O bonds of methoxycarbonyl groups.

Analysis of the mass spectra of thiopyrans **5a—i** and **8b** (Scheme 3, see Table 5) revealed the following major routes of fragmentation upon electron impact: abstraction of the substituent R^2 (Φ_2) and R^4 (Φ_3), ejection of the isothiocyanate molecule (Φ_4), and elimination of sulfur from the ring to give fragments related to other types of destruction of the thiopyran ring.

It is noteworthy that the ^{1}H NMR spectrum of methyl 6-amino-5-cyano-4*H*-thiopyran-3-carboxylates (R^4 = H; compounds **5a,d,h, 6b,d, 7b, 9**), resulting from the reaction of thioacrylamides **4** with an unsymmetrical dienophile, methyl propiolate, displays only one set of signals for all proton-containing groups, the signals for the thiopyran ring protons being represented by two separate singlets. This indicates that the process is highly selective and gives, of the two possible regiosomers **11** and **12**, only the former one.

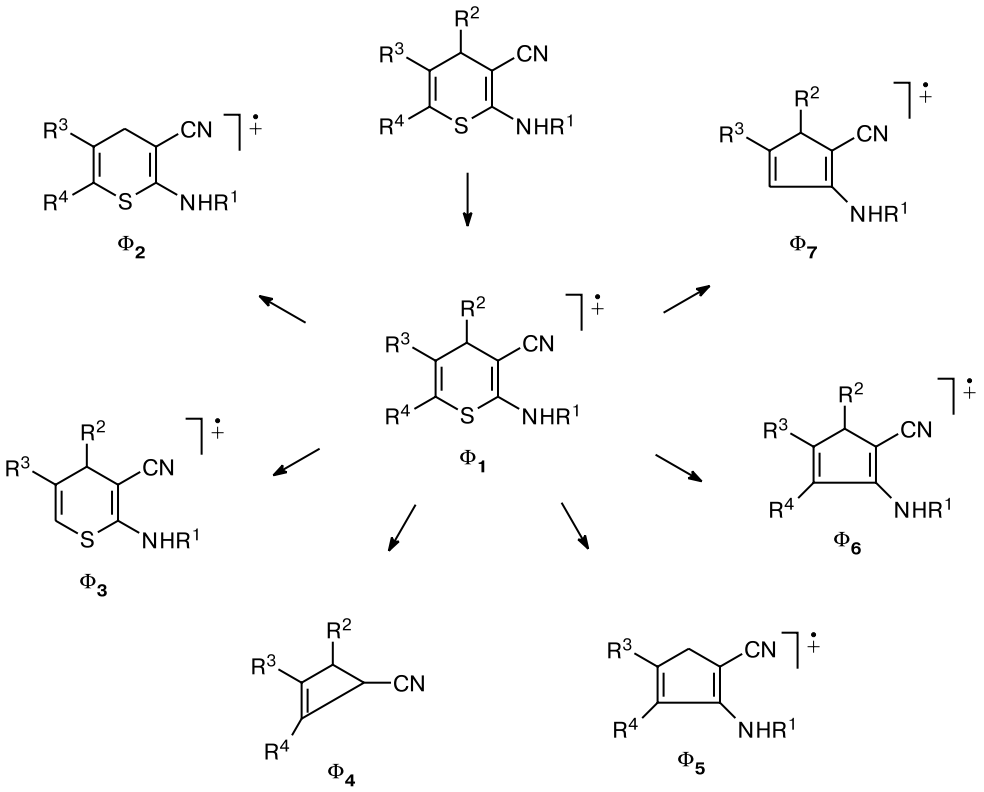


11 **12**

Table 5. Mass spectrometry data for 6-amino-4-aryl-5-cyano-4*H*-thiopyrans **5a—i** and **8b**

Compound	*m/z* (I_{rel} (%))						
	Φ_1	Φ_2	Φ_3	Φ_4	Φ_5	Φ_6	Φ_7
5a	364 (12.6)	305 (100.0)	253 (34.9)	306 (17.6)	333 (7.2)	221 (5.1)	273 (0.0)
5b	306 (25.8)	195 (100.0)	247 (30.8)	247 (30.8)	162 (0.0)	274 (0.0)	215 (0.0)
5c	446 (17.4)	335 (100.0)	387 (78.5)	305 (47.1)	302 (0.0)	415 (4.4)	355 (1.9)
5d	388 (44.7)	277 (88.9)	329 (19.0)	247 (17.2)	244 (0.0)	356 (0.0)	356 (0.0)
5e	432 (23.9)	321 (29.6)	373 (100.0)	321 (29.6)	288 (0.0)	401 (7.5)	341 (4.1)
5f	462 (13.9)	351 (31.9)	403 (100.0)	306 (0.0)	319 (5.9)	430 (0.0)	371 (2.6)
5g	378 (12.3)	267 (41.2)	319 (100.0)	305 (2.6)	235 (8.1)	346 (6.6)	287 (4.8)
5h	320 (25.0)	209 (100.0)	261 (22.1)	247 (1.4)	177 (10.8)	288 (5.2)	230 (0.0)
5i	418 (18.7)	307 (20.0)	359 (100.0)	305 (49.3)	274 (0.0)	386 (0.0)	327 (5.0)
8b	456 (13.1)	335 (2.9)	397 (100.0)	314 (0.0)	303 (2.1)	424 (0.0)	365 (1.2)

Scheme 3



The reaction of cyanothioacrylamides **4c,i,j,l** with phenylmaleimide was carried out under similar conditions using a threefold excess of the dienophile. Hexahydrothiopyrano[2,3-*d*]pyrrolecarbonitriles **10** were formed in 56 to 62% yields.

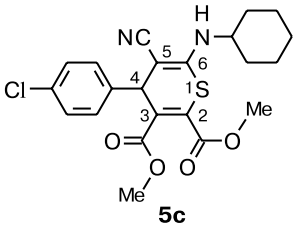
The ^{1}H NMR spectra of bicyclic compounds **10** differ from the spectra of 4*H*-thiopyrans **5—9** by the presence of three groups of signals of coupled protons. Thus the CH protons in the bridgehead positions of thiopyranopyrroles **10** are responsible for a doublet of doublets with δ 3.91—4.26 and a doublet a δ 4.10—4.44. The coupling constants of two pairs of protons (C(3)—C(2), C(4)—C(3)) are substantially different, being equal to 8.7—9.9 and 2.6—5.5 Hz, respectively, which may imply the axial positions of C(2)—C(3) protons and an equatorial position of the C(4) proton. The lack of additional signals in the ^{1}H NMR spectrum attests to the formation of only one of four possible diastereomers and is a distinctive feature of cyanothioacrylamides with respect to thioacrylamides.[6] For the latter compounds, the formation of two diastereomeric adducts with different spatial positions of substituents in the ring was detected in the reaction with *N*-phenylmaleimide. This high process stereoselectivity can be due to additional spatial interactions in the transition state caused by the presence of the cyano group,[6] because variation of other structural factors does not result in any substantial changes in the conformation of the reaction products. The characteristic signals in the ^{13}C NMR spectra correspond to the carbon atoms in positions 2, 3, and 4 of the thiopyran fragment; they occur at δ 44.6—47.5 and show appropriate splitting (Table 6).

As a result of this study, we synthesized a series of new mono- and bicyclic thiopyrans. The variation of substituents having different electronic and steric effects in the thiocabamoyl group and the substituent in position 3 of the 1-thiabuta-1,3-diene system did not exert any substantial effect on the nature of the products, reaction conditions, product yields or process duration. The presence of a cyano group in the α′-position of thioacrylamides is the most important factor, resulting in cycloaddition without additional activation by acylation or the use of catalysts. Moreover, this structural modification of thioacrylamides increases the regioselectivity and stereoselectivity of the reaction.

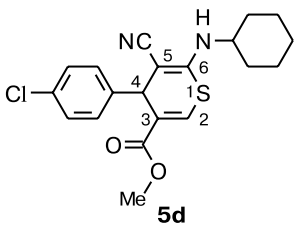
Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Bruker WM-250 instrument (^{1}H, 250.13 MHz; ^{13}C, 100.00 MHz) in a $CDCl_3$ solution using Me_4Si as the internal standard. The reactions were monitored and the product purity was checked by

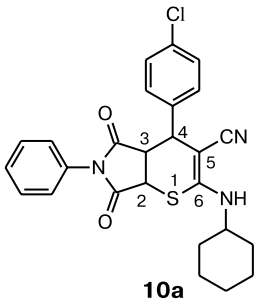
Table 6. ^{13}C NMR data for 6-amino-4-aryl(hetaryl)-5-cyanothiopyrans **5c,d** and thiopyranopyrrole **10a**



5c



5d



10a

Compound	δ (*J*/Hz)								
	R^2	C(2)	C(3)	C(4)	C(5) (m)	C(6)	CN	*cyclo*-C_6H_{11}	R^4, R^3
5c	154.2 (dt, J_1 = 6.7, J_2 = 2.8); 132.3 (tt, J_1 = 13.8, J_2 = 3.5); 128.8 (dd, J_1 = 168.4, J_2 = 5.0); 128.5 (ddd, J_1 = 162.0, J_2 = 7.1, J_3 = 0.8)	138.6 (q, J = 7.4)	130.0 (d, J = 6.7)	44.5 (dt, J_1 = 134.7, J_2 = 3.9)	69.3	132.7 (d, J = 8.2)	119.7 (d, J = 5.1)	54.1 (d, J = 137.9); 33.1, 32.7, 24.8, 24.4, 24.3 (all t, J = 130.3)	164.8 (dq, J = 4.1); 163.1 (q, J = 3.3); 53.6, 52.0 (both q, J_1 = 149.9)
5d	151.9 (m); 131.8 (tt, J_1 = 10.8, J_2 = 3.2); 128.7 (dd, J_1 = 166.9, J_2 = 5.4); 128.5 (ddd, J_1 = 162.0, J_2 = 7.1, J_3 = 0.8)	130.8 (dd, J_1 = 182.7, J_2 = 5.8)	141.5 (dq, J_1 = 7.2, J_2 = 1.2)	41.7 (ddt, J_1 = 134.3, J_2 = 6.7, J_3 = 3.8)	70.5	131.0 (d, J_1 = 5.9)	120.2 (d, J = 4.4)	53.8 (d, J = 135.3); 33.1, 32.9, 24.8, 24.6, 24.4 (all t, J = 130.3)	163.5 (ddq, J_1 = 3.8, J_2 = 3.5, J_3 = 1.9); 52.3 (q, J = 146.8); 41.7 (m)
10a	157.9, 131.8 (both m); 129.1 (dd, J_1 = 161.0; J_2 = 7.0); 128.7 (dd, J_1 = 166.0, J_2 = 5.2)	45.8 (dd, J_1 = = 151.7) J_2 = 5.4)	47.5 (ddd, J_1 = = 142.6, J_2 = 6.3, J_3 = 2.5)	44.6 (d, J = 131.4)	71.9	136.4 (dd, J_1 = 7.3, J_2 = 8.0)	118.9 (d, J = 4.8)	53.8 (d, J = 137.8); 33.1, 24.8, 24.6, 24.5 (all t, J = 130.3)	174.3 (m); 173.8 (dd, J_1 = 5.4, J_2 = 3.8); 131.9 (ddd, J_1 = 162.7, J_2 = 5.2, J_3 = 2.1); 131.6 (dt, J_1 = 161.1, J_2 = 7.7); 127.7 (d, J = 163.3); 126.6 (m)

TLC on Sorbfil UV-254 plates in an ethyl—hexane (1 : 1) mixture. Mass spectra were run on a Varian MATT 311A instrument with an ionizing voltage of 3 kV and an ionization energy of 70 eV. Melting points were not corrected.

The yields and the physicochemical characteristics of the synthesized compounds are presented in Tables 1—6.

Preparation of 3-aryl(hetaryl)-2-cyanoacrylamides 3 (general procedure). Method *A*. Aldehyde (6.0 mmol), 2-cyanoacetamide (6.6 mmol), and piperidine (0.02 g, 0.24 mmol) were refluxed for 15 h in toluene (30 mL). The reaction mixture was cooled to room temperature. The precipitate was filtered off.

Method *B*. Aldehyde (6.0 mmol) and 2-cyanoacetamide (6.6 mmol) were fused together at 150 °C. The resulting material was recrystallized from ethanol.

Synthesis of 3-aryl(hetaryl)-2-cyanothioacrylamides 4 (general procedure). Method *C*. 3-Aryl(hetaryl)-2-cyanoacrylamide (3.5 mmol) and the Lawesson´s reagent (0.707 g, 1.75 mmol) were refluxed for 10 h in toluene (30 mL). Toluene was evaporated *in vacuo*. The residue was recrystallized from EtOH.

Method *D*. Aldehyde (6.0 mmol), 2-cyanothioacetamide (6.6 mmol), and *N*-methylmorpholine (0.242 g, 0.24 mmol) were kept for 15 h in EtOH (30 mL) at room temperature. The precipitate was filtered off.

Preparation of 6-amino-4-aryl(hetaryl)-5-cyanothiopyrans 5—9 and 2-amino-4-aryl(hetaryl)-5,7-dioxo-6-phenyl-4,4a,5,6,7,7a-hexahydrothiopyrano[2,3-*c*]pyrrole-3-carbonitriles 10 (general procedure). 3-Aryl(hetaryl)-2-cyanothioacrylamide (0.48 mmol) and dienophile (2.4 mmol) were re-

fluxed for 2—5 h in *m*-xylene (10 mL). The solvent was evaporated *in vacuo* and the oily residue was recrystallized from MeOH.

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