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SYNTHESIS AND INVESTIGATION OF SOME 1,4-DISUBSTITUTED 2-PYRROLIDINONES

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A series of condensation products of 1-aryl-4-hydrazinecarbonyl-2-pyrrolidinones with acetone, 2,4-pentanedione, and aromatic aldehydes was obtained and identified by the combination of IR, mass and ^{1}H, ^{13}C NMR spectroscopy. The results of their structural studies by NMR spectroscopy are provided. It was ascertained that the presence of the NH group determines the existence of the mixtures of the Z/E-isomers of compounds under study. The availability of Z-isomer as a sterically favorable one was also verified by computer molecular modeling.

Keywords: 1-aryl-4-hydrazinecarbonyl-2-pyrrolidinones, hydrazones, *Z/E*-isomers, pyrazoles, condensation, spectroscopy.

The products of condensation of carbohydrazides with carbonylic compounds – hydrazones – and its ring-closure reactions are well known and have been thoroughly studied. Compounds of these types are important for both chemical and pharmacological purposes and show analgetic, antidepressive, and bactericidal activities [1]. 1-Aryl-substituted 4-carboxy-2-pyrrolidinones and their salts, esters, amides, and nitriles are plant growth stimulators [2]. The first nucleophilic reaction used in this work was hydrazinolysis of the ester function. Acid hydrazides **2a-c** were prepared from the corresponding esters **1a-c** and hydrazine monohydrate in refluxing 2-propanol (Scheme 1).

Condensation of compounds **2a-c** with acetone gave the corresponding isopropylidenehydrazine-carbonyl-2-pyrrolidinones **3a-c**, and the one – **2b** with aromatic aldehydes – 1-aryl-4-arylidenehydrazine-carbonyl-2-pyrrolidinones **5-9**. 1-Aryl-4-[(3,5-dimethylpyrazol-1-yl)carbonyl]-2-pyrrolidinones **4a-c** were synthesized by condensation of hydrazides **2a-c** with 2,4-pentanedione in 2-propanol in the presence of a catalytic amount of hydrochloric acid.

N-Substituted hydrazones **10-12** were obtained in good yields by alkylation of 1-aryl-4-arylidenehydrazinecarbonyl-1-pyrrolidinones **5**, **6** and **8** with ethyl iodide in the presence of potassium hydroxide and potassium carbonate with excess of ethyl iodide without solvent.

The structure of the studied compounds **3-12** was elucidated by the methods of IR, mass and ^{1}H, ^{13}C NMR spectroscopy. Because of the different nature of fragments of the molecules of the tentative compounds their structural features were mostly unfolded by ^{1}H, ^{13}C NMR spectroscopy. Investigation of such structural fragments revealed information concerning the relation between the effects of substituents, their steric arrangement, and the possibility to participate in hydrogen bonding and conjugation. The signals in the NMR spectra were assigned [3, 4] on the basis of chemical shift theory, multiplicities, signal intensities, and comparison with suitable model compounds. The assignment was confirmed by ^{13}C NMR APT spectra. The results obtained are given in Tables 2-5. The identification of aromatic carbons in the ^{13}C NMR spectra

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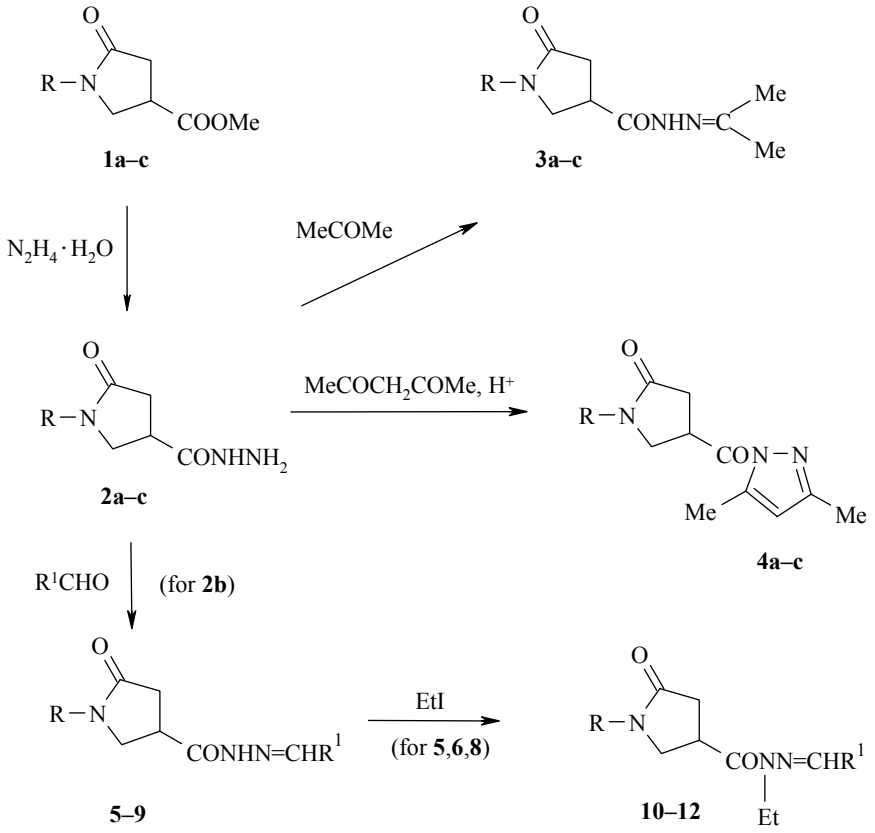
presented some difficulties due to the unknown pyrrolidinone ring influence. Therefore, the model compound (4-isopropylidenehydrazinecarbonyl-1-phenyl-2-pyrrolidinone) was synthesized, and the increments of the pyrrolidinone ring for benzene carbons were calculated (Δδ: C_i = 10.72, C_o = -9.07, C_m = 0.11, C_p = -4.52 ppm) and proved to be useful for the prediction of the chemical shifts of benzene carbons in other compounds under study. Probably due to the hindered rotation around the C(1')–N(1) bond, in compounds **3c** and **4c** with 3,5-$Me_2C_6H_3$ substitution the C-5 atom in pyrrolidinone ring is deshielded about 2 ppm, the C-2 atom shielded about 0.5 ppm, and the C-4 atom in compound **4c** – shielded about 1.5 ppm compared with suitable effects in compounds **3a**,**b**, **4a**,**b** with 3-Me and 4-Me substituents in the benzene ring.



1-4 a R = 3-MeC_6H_4, **b** R = 4-MeC_6H_4, **c** R = 2,5-MeC_6H_3; **5-12** R = 4-MeC_6H_4;
5, **11** R^1 = 4-BrC_6H_4, **6**, **10** R^1 = 4-$O_2NC_6H_4$, **7** R^1 = 4-HOC_6H_4,
8, **12** R^1 = 4-$Me_2NC_6H_4$, **9** R^1 = 9-ethyl-3-carbazolyl

The tentative compounds **3a-c**, **5-9** exhibit characteristic structural features due to the presence of the azomethine fragment (C=N) [5-7], on the one hand, and the amide group (CO–NHR) [4, 5] on the other hand. Due to the possibility of a different arrangement of the substituents with respect to the C=N fragment or carbonyl oxygen in the amide group, the existence of two isomers is possible. Such steric structural changes are well reflected in the NMR spectra.

There are many works published on the structure and spectroscopic properties of hydrazones and amides [8-12]. In this paper we describe compounds **3a-c**, **5-9** which have shown two sets of some resonances. Numerous attempts have been made to analyze compounds **3a-c** which possess two Me substituents in the N=C fragment. Thus, a double set of resonances in this case is observed due to the features of the amide group. Fragment N=C$(CH_3)_2$ may be displaced as *Z* or *E* with respect to carbonyl oxygen atom [4, 5, 10-12]. When the mentioned fragment is located as *E*, H of the hydrazide group is turned as *Z*. Such a situation is favorable for

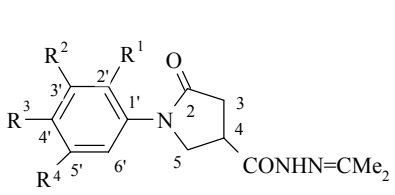
formation of internal hydrogen bonding [13, 14]. The resonances of carbon atoms sensitive to such structural changes are shifted downfield. As a result of hydrogen bond formation, the carbonyl group carbon is more positively charged as its deshielding is observered (found at ~173 ppm). Otherwise, when fragment $N=C(CH_3)_2$ is in the *Z*-position, there is no possibility for internal hydrogen bonding between CO and NH groups. In this case the geometrical isomer, which resonance signals are shifted upfield, is obtained. The carbonyl group carbon atoms in these isomers resonate at 168 ppm. The studied compounds **5-9** exhibit a double set of resonances, which may be due to the presence of the amide group as well as different arrangement of substituents with respect to the N=C group (*Z/E*-forms), because the mentioned compounds possess dissimilar substitution in the N=C group. Differences in the chemical shifts of compounds **3a-c** are observed for CO (about 5.1) and N=C (about 5.0), for C-4 (1.4), C-3 (0.9), C-5 (0.6), C-2 (0.1), CH_3 (0.3 ppm). The differences in the chemical shifts of compounds **5-9** are the following: for CO (about 4.9) and N=C (about 3.3), for C-4 (2), C-3 (0.7), C-5 (0.4), C-2 (0.2 ppm).

TABLE 1. Data of Compounds **2-4** and **5-12**

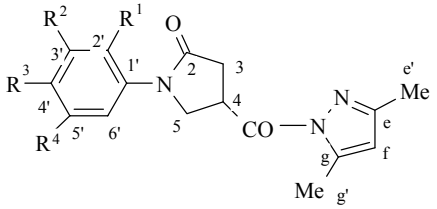
Compound	Empirical formula	Found, % / Calculated, %			mp, °C*	Yield, %
		C	H	N		
2a	$C_{12}H_{15}N_3O_2$	61.05 / 61.79	6.77 / 6.48	18.29 / 18.01	216-217	85
2b	$C_{12}H_{15}N_3O_2$	61.77 / 61.79	5.8 / 6.48	18.36 / 18.01	181-182	79.4
2c	$C_{13}H_{17}N_3O_2$	63.09 / 63.14	6.63 / 6.93	16.27 / 16.99	140-141	40.2
3a	$C_{15}H_{19}N_3O_2$	65.91 / 65.91	6.4 / 7.01	15.47 / 15.37	167-168	71
3b	$C_{15}H_{19}N_3O_2$	66.09 / 65.91	6.80 / 7.01	15.55 / 15.37	100-101	40.5
3c	$C_{16}H_{21}N_3O_2$	66.53 / 66.88	7.15 / 7.37	14.73 / 14.62	132-133	35.2
4a	$C_{17}H_{19}N_3O_2$	69.01 / 68.67	6.21 / 6.44	13.41 / 14.13	115-116	52.4
4b	$C_{17}H_{19}N_3O_2$	68.53 / 68.67	6.23 / 6.44	13.95 / 14.13	124-125	78.5
4c	$C_{18}H_{21}N_3O_2$	69.98 / 69.43	6.80 / 6.68	13.49 / 13.28	125-126	40
5	$C_{19}H_{18}BrN_3O_2$	57.06 / 57.01	4.85 / 4.53	10.36 / 10.50	246-247	91.5
6	$C_{19}H_{18}N_4O_4$	62.04 / 62.29	5.10 / 4.95	15.42 / 15.29	228-229	91.5
7	$C_{19}H_{19}N_3O_3$	67.34 / 67.64	5.32 / 5.68	12.23 / 12.45	205-206	69.6
8	$C_{21}H_{24}N_4O_2$	69.37 / 69.21	6.52 / 6.64	15.37 / 15.37	210-211	92.1
9	$C_{27}H_{26}N_4O_2$	73.58 / 73.95	7.66 / 5.98	12.53 / 12.78	224-225	88.6
10	$C_{21}H_{22}N_4O_4$	63.83 / 63.95	5.40 / 5.62	13.99 / 14.20	216-217	65
11	$C_{21}H_{22}BrN_3O_2$	58.42 / 58.89	5.55 / 5.18	9.76 / 9.81	175-176	53
12	$C_{23}H_{28}N_4O_2$	70.82 / 70.38	7.43 / 7.19	14.30 / 14.27	152-153	66.7

* Solvent for crystallization: 2-propanol (compounds **2a-c**, **3a-c**, **4b**, **9-12**), ethanol (compounds **5-8**), acetone (compound **3b**), toluene (compounds **4a,c**).

TABLE 2. ^{13}C NMR Spectral Data of Compounds **3a-c**, **4a-c**



3a-c



4a-c

a $R^1 = R^3 = R^4 = H$, $R^2 = Me$; **b** $R^1 = R^2 = R^4 = H$, $R^3 = Me$; **c** $R^1 = R^4 = Me$; $R^2 = R^4 = H$

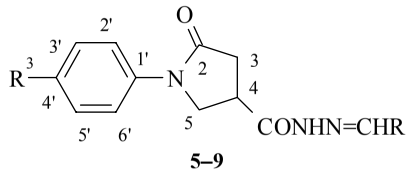
Carbon atoms	δ, ppm (DMSO-d_6)								
	3a		**3b**		**3c**		**4a**	**4b**	**4c**
	E	*Z*	*E*	*Z*	*E*	*Z*			
C-1'	139.18		136.78		137.29		138.98	136.58	137.04
C-2'	120.01	119.94	119.44	119.33	130.54		120.10	119.54	130.42
C-3'	137.90		129.04		132.15		137.92	129.03	132.14
C-4'	124.68		133.02		128.18		124.68	133.21	128.14
C-5'	128.46		129.04		135.71		128.44	129.03	135.74
C-6'	116.69	116.57	119.44	119.33	127.06	126.99	116.78	119.54	126.99
C-2	172.03	171.92	171.84	171.74	171.53	171.45	171.39	171.20	170.85
C-3	35.86	34.99	35.78	34.90	35.54	34.37	35.36	35.35	36.50
C-4	34.31	32.91	34.30	32.90	34.06	33.38	35.09	35.04	33.65
C-5	50.87	50.24	50.83	50.21	52.64	52.12	50.21	50.15	51.95
C=O	173.63	168.52	173.64	168.56	173.81	168.73	172.57	173.33	172.79
N=C	156.17	151.19	156.15	151.18	156.05	151.07			
CH_3	17.59	17.19	17.59	17.08	25.18	17.54			
	25.23	24.92	24.92	25.22	17.98	24.91			
2'-CH_3					15.12				17.02
3'-CH_3	21.16						21.12		
4'-CH_3			21.37					20.37	
5'-CH_3					20.28				20.26
C-e							152.09	152.08	152.01
C-f							111.53	111.53	111.50
C-g							143.83	143.83	143.79
C-e'							13.99 or 13.53	13.99 or 13.53	14.02 or 13.48
C-g'							13.99 or 13.53	13.99 or 13.53	14.02 or 13.48

Direct comparison of the data obtained from these examinations shows remarkably similar changes in the chemical shifts. The most significant differences are for the same carbons, which are mostly affected due to the steric perturbations. The differences in the chemical shifts become smaller or disappear completely for carbons that are more distant from the center of the exchanges.

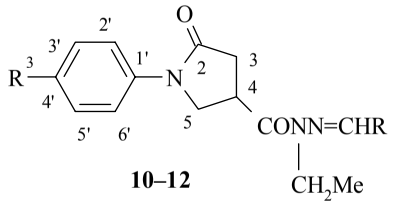
Only one set of resonances is present in the spectra of compounds **10-12**. These compounds are the corresponding alkylated derivatives of **6**, **5**, **8**, and the NH group with mobile H is absent in their molecules. Apparently, the presence of the NH group in compounds **3a-c** and **5-9** causes the stabilization of some steric structures, which are reflected in the NMR spectra.

It has been noted that the ^{13}C NMR spectra of compounds **4a-c** do not show splitting of the resonances. Such spectral data are assigned in detail – the signals are resolved sufficiently to permit individual identification

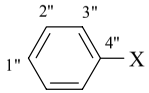
TABLE 3. ^{13}C NMR Spectral Data of Compounds **5-12***

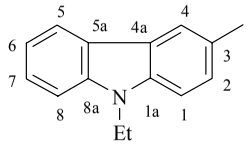


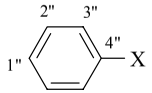
5–9



10–12

5–8 R = 

9 R = 

R = 

5 X = Br, **6** X = NO_2, **7** X = OH, **8** X = NMe_2

10 X = NO_2, **11** X = Br, **12** X= NMe_2

Carbon atoms	δ, ppm (DMSO-d_6)																	
	5		**6**		**7**		**8**		**9**		**10**	**11**	**12**
	E	*Z*	*E*	*Z*	*E*	*Z*	*E*	*Z*	*E*	*Z*			
1	2	3	4		5		6	7	8		9	10	11
C-1'	136.74	136.68	136.74		136.78		136.80	136.72	136.82		136.70	136.73	136.78
C-2'	119.46	119.39	119.49	119.41	119.49	119.39	119.44	119.37	119.40	119.39	119.45	119.44	119.40
C-3'	129.04		129.05		129.05		129.04		129.06		129.02	129.02	129.01
C-4'	133.39		133.12		133.06		133.06	133.03	133.09		133.09	133.06	132.99
C-5'	129.04		129.05		129.05		129.04		129.06		129.02	129.02	129.01
C-6'	119.46	119.39	119.49	119.41	119.49	119.39	119.44	119.37	119.40	119.39	119.45	119.44	119.40

TABLE 3 (continued)

1	2	3	4		5		6	7	8		9	10	11
C-2	171.69	171.51	171.63	171.45	171.83	171.63	171.84	171.64	171.87	171.64	171.61	171.68	171.82
C-3	35.57	34.86	35.40		35.66	34.89	35.69	34.88	35.35		35.59	35.25	34.85
C-4	34.80	32.78	34.48	32.82	34.77	32.80	34.76	32.83	35.04		33.30	33.30	33.46
C-5	50.47	50.03	50.40	49.97	50.60	50.14	50.64	50.19	50.65	50.22	50.37	50.46	50.80
C=O	173.61	168.75	173.96	169.13	173.16	168.26	172.87	167.99	173.27	168.33	173.09	172.76	172.02
N=CH	145.74	142.43	147.85	144.53	147.29	143.89	147.78	144.38	148.21	144.88	138.19	139.24	140.99
C-1"	133.07		140.45	140.39	125.12		121.49	121.33			141.06	134.09	125.12
C-2"	128.90	128.73	127.98	127.82	128.81	128.56	128.37	128.08			127.94	128.92	122.29
C-3"	131.77		124.09	123.99	115.66		111.79	111.73			123.99	131.75	128.27
C-4"	123.30	123.04	147.85	147.68	159.42	159.21	151.49	151.33			147.54	122.83	111.77
2'-CH_3	20.38		20.38		20.40		20.38		20.39		20.35	20.36	20.40
$N(CH_3)_2$							39.73				35.30, 10.72	35.32, 10.82	35.33, 11.11
$N\underline{CH_2}CH_3$									37.11	37.04			39.73
$NCH_2\underline{CH_3}$									13.71				

* Compounds **5-9**: ^{13}C NMR chemical shifts of carbazole rings C-3 – 124.51 or 124.07, C-2 – 126.45 or 126.15, C-1 – 109.41, C-1a – 140.44, C-4a – 120.68 or 120.60, C-4 – 122.09, C-5 – 120.23, C-6 – 119.06, C-7 – 125.10 or 105.04, C-8 – 109.58, C-8a – 139.94.

TABLE 4. ^{1}H NMR Spectra of Compounds **3-12**

Compound	Chemical shifts, coupling constants, δ, ppm (*J*, Hz)
3a	1.87, 1.88, 1.93, 1.93 (6H, 4s, *Z/E* N(CH_3)$_2$); 2.30 (3H, s, 3'-CH_3); 2.60-2.79 (2H, m, $^2J_{HCH}$ = 16.9, $^3J_{HCCH}$ = 7.2, $^3J_{HCCH}$ = 9.2, CH_2CO); 3.36-3.47 (0.5H, m, CH); 3.83-4.07 (2H, m, CH_2N and 0.5 H, m, CH); 6.94-7.46 (4H, m, Ar); 10.20, 10.30 (1H, 2s, *Z/E* NH)
3b	1.87, 1.88, 1.93, 1.93 (6H, 4s, *Z/E* N(CH_3)$_2$); 2.27 (3H, s, 4'-CH_3); 2.59-2.78 (2H, m, $^2J_{HCH}$ = 16.9; $^3J_{HCCH}$ = 7.2, $^3J_{HCCH}$ = 9.2, CH_2CO); 3.36-3.47 (0.4H, m, CH); 3.81-4.08 (2H, m, CH_2N and 0.6H, m, CH); 7.16 (2H, d, *J* = 7.6, H-2',6'); 7.52 (2H, d, *J* = 7.6, m, H-3',5'); 10.20, 10.29 (1H, 2s, *Z/E* NH)
3c	1.88, 1.89, 1.93, 1.95 (6H, 4s, *Z/E* N(CH_3)$_2$); 2.10, 2.12 (3H, 2s, 3'-CH_3); 2.28 (3H, s, 5'-CH_3); 2.55-2.73 (2H, m, $^2J_{HCH}$ = 16.9, $^3J_{HCCH}$ = 7.2, $^3J_{HCCH}$ = 9.2, CH_2CO); 3.30-3.55 (0.4H, m, CH); 3.65-4.05 (2H, m, CH_2N and 0.6H, m, CH); 7.04-7.21 (4H, m, Ar); 10.19, 10.28 (1H, 2s, *Z/E* NH)
4a	2.21, 2.30 (6H, 2s, e'-, g'-CH_3); 2.48 (3H, s, 3'-CH_3); 2.77-2.94 (2H, m, $^2J_{HCH}$ = 10.2, $^3J_{HCCH}$ = 6. 9; $^3J_{HCCH}$ = 9.1, CH_2CO); 3.98-4.22 (2H, m, $^2J_{HCH}$ = 10.2, $^3J_{HCCH}$ = 5.3, $^3J_{HCCH}$ = 8.8, CH_2N); 4.42-4.52 (1H, m, $CH_2\underline{CH}CH_2$); 6.22 (1H, s, CH=); 6.94-7.46 (4H, m, Ar)
4b	2.20, 2.27 (6H, 2s, e'-, g'-CH_3); 2.48 (3H, s, 4'-CH_3); 2.76-2.84 (2H, m, $^2J_{HCH}$ = 17.2; $^3J_{HCCH}$ = 6.9, $^3J_{HCCH}$ = 9.1, CH_2CO); 3.97-4.22 (2H, m, $^2J_{HCH}$ = 17.2, $^3J_{HCCH}$ = 5.6; $^3J_{HCCH}$ = 8.9, CH_2N); 4.45-4.52 (1H, m, $CH_2\underline{CH}CH_2$); 6.23 (1H, s, CH=); 7.16 (2H, d, *J* = 8.4, H-2',6'); 7.52 (2H, d, *J* = 8.4, H-3',5')
4c	2.09, 2.18 (6H, 2s, e'-, g'-CH_3); 2.26 (3H, s, 3'-CH_3); 2.47 (3H, s, 5'-CH_3); 2.70-2.89 (2H, m, $^2J_{HCH}$ = 17.2, $^3J_{HCCH}$ = 8.6, $^3J_{HCCH}$ = 9.2, CH_2CO); 3.79-4.08 (2H, m, $^2J_{HCH}$ = 9.9, $^3J_{HCCH}$ = 5.3; $^3J_{HCCH}$ = 9.5, CH_2N); 4.47-4.57 (1H, m, $CH_2\underline{CH}CH_2$); 6.22 (1H, s, CH=); 7.02-7.16 (3H, m, Ar)
5	2.28 (3H, s, 4'-CH_3); 2.65-2.91 (2H, m, $^2J_{HCH}$ = 16.9, $^3J_{HCCH}$ = 7.4, $^3J_{HCCH}$ = 9.8, CH_2CO); 3.29-3.43 (1H, m, $CH_2\underline{CH}CH_2$); 3.90-4.17 (2H, m, CH_2N); 7.15-7.69 (4H, m, Ar); 8.01, 8.20 (1H, 2s, *Z/E* CH=); 11.64, 11.70 (1H, 2s, *Z/E* NH)
6	2.28 (3H, s, 4'-CH_3); 2.69-2.90 (2H, m, $^2J_{HCH}$ = 17.0, $^3J_{HCCH}$ = 7.3, $^3J_{HCCH}$ = 9.8**,** CH_2CO); 3.26-3.44 (1H, m, $CH_2\underline{CH}CH_2$); 3.94-4.20 (2H, m, CH_2N); 7.54-8.30 (4H, m, Ar); 7.80, 8.14 (1H, 2s, *Z/E* CH=); 11.86, 11.93 (1H, 2s, *Z/E* NH)
7	2.28 (3H, s, 4'-CH_3); 2.66-2.86 (2H, m, $^2J_{HCH}$ = 16.9, $^3J_{HCCH}$ = 7.6, $^3J_{HCCH}$ = 9.4**,** CH_2CO); 3.26-3.42 (1H, m, $CH_2\underline{CH}CH_2$); 3.90-4.14 (2H, m, CH_2N); 6.80-7.56 (4H, m, Ar); 7.94, 8.11 (1H, 2s, *Z/E* CH=); 9.89 (1H, s, OH); 11.36, 11.42 (1H, 2s, *Z/E* NH)
8	2.28 (3H, s, 4'-CH_3); 2.95, 2.96 (6H, 2s, N(CH_3)$_2$); 2.66-2.82 (2H, m, $^2J_{HCH}$ = 16.9, $^3J_{HCCH}$ = 7.6; $^3J_{HCCH}$ = 9.8**,** CH_2CO); 3.25-3.39 (1H, m, $CH_2\underline{CH}CH_2$); 3.90-4.10 (2H, m, CH_2N); 6.71-7.56 (4H, m, Ar); 7.91, 8.08 (1H, 2s, *Z/E* CH=); 11.28, 11.33 (1H, 2s, *Z/E* NH)
9	1.32 (3H, t, *J* = 6.9, $NCH_2\underline{CH_3}$); 2.28 (3H, s, 4'-CH_3); 2.71-2.94 (2H, m, $^2J_{HCH}$ = 17.0, $^3J_{HCCH}$ = 7.7, $^3J_{HCCH}$ = 8.9, CH_2CO); 3.27-3.49 (1H, m, $CH_2\underline{CH}CH_2$); 3.94-4.23 (2H, m, CH_2N); 4.43 (2H, q, *J* = 6.9, $N\underline{CH_2}CH_3$); 7.16-8.46 (4H, m, Ar); 7.87, 7.90 (1H, 2s, *Z/E* CH=); 11.51, 11.57 (1H, 2s, *Z/E* NH)
10	1.14 (3H, t, *J* = 7.0, $NCH_2\underline{CH_3}$); 2.28 (3H, s, 4'-CH_3); 2.76-2.92 (2H, m, $^2J_{HCH}$ = 9.8, $^3J_{HCCH}$ = 6.0, $^3J_{HCCH}$ = 9.6**,** CH_2CO); 3.90-4.19 (2H, m, $^2J_{HCH}$ = 9.8, $^3J_{HCCH}$ = 7.6, $^3J_{HCCH}$ = 9.2**,** CH_2N); 4.08 (2H, q, *J* = 7.0, $N\underline{CH_2}CH_3$); 4.30-4.41 (1H, m, $CH_2\underline{CH}CH_2$); 7.13-8.33 (4H, m, Ar); 8.26 (H, s, CH=)
11	1.12 (3H, t, *J* = 7.0, $NCH_2\underline{CH_3}$); 2.28 (3H, s, 4'-CH_3); 2.74-2.89 (2H, m, $^2J_{HCH}$ = 17.3, $^3J_{HCCH}$ = 7.8, $^3J_{HCCH}$ = 8.9, CH_2CO); 3.92-4.16 (2H, m, $^2J_{HCH}$ = 9.8, $^3J_{HCCH}$ = 6.1, $^3J_{HCCH}$ = 9.0, CH_2N); 4.05 (2H, q, *J* = 7.0, $N\underline{CH_2}CH_3$); 4.26-4.37 (1H, m, $CH_2\underline{CH}CH_2$); 7.17-7.80 (4H, m, Ar); 8.11 (1H, s, CH=)
12	1.08 (3H, t, *J* = 7.1, $NCH_2\underline{CH_3}$); 2.29 (3H, s, 4'-CH_3); 2.97 (6H, s, N(CH_3)$_2$); 2.80, 2.83 (2H, d, $^3J_{HCCH}$ = 8.4**,** CH_2CO); 3.91-4.16 (2H, m, $^2J_{HCH}$ = 9.6, $^3J_{HCCH}$ = 6.1, $^3J_{HCCH}$ = 9.0, CH_2N); 4.03 (2H, q, *J* = 7.1, $N\underline{CH_2}CH_3$); 4.20-4.31 (1H, m, $CH_2\underline{CH}CH_2$); 6.75-7.65 (4H, m, Ar); 7.98 (1H, s, CH=)

of each carbon [15-17]. The characteristic resonances found at 152, 143 and 111 ppm are assigned to suitable carbons of the pyrrazole ring.

Considerable attention has been paid to the ^{1}H NMR spectra of the compounds under study [4, 5]. The ^{1}H NMR spectra of compounds **4a-c** demonstrate the presence of a characteristic signal at 6.22 ppm, which confirms the existence of the pyrrazole ring. The spectra of compounds **3a-c** possess two signals of the NH

group of equal intensity, indicating the same possibility for two different isomers to exist. Two resonances of the NH group appear in compounds **5-9**, and their intensity relationships can be expressed quantitatively: 30%:70%. These observations indicate the existence of *E*- and *Z*-isomers, and meanwhile show that the *Z*-isomer is predominant against the *E*-isomer. Computer molecular modeling applied to the structural studies of these compounds has shown the same trend.

The ^{1}H NMR multiplets of the pyrrolidinone ring of compounds **3a-c**, **5-9** are complex and difficult to resolve [18]. The integral intensity is not distributed evenly in accordance with the number of protons of the $COCH_2$, CH, NCH_2 fragments. Their chemical shifts, multiplicity, and integral intensity change significantly due to the sensitivity of the influence of substituents, formation of extended π-system between the benzene fragment and the N(1)–C(2) bond, and formation of the different isomers in the side chain of the ring.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Unity Inova 300 (300 MHz) spectrometer operating in Fourier transform mode with TMS as an internal standard. Melting points were determined on an automatic melting point apparatus APA1 and are uncorrected. The IR spectra were determined in potassium bromide pellets on a Perkin-Elmer FT-IR system spectrum GX spectrometer. Mass spectral data were obtained by a Waters (Micromas) ZQ 200 Spectrometer.

The molecular formulas of the studied compounds, data of elemental analysis, and magnitudes of the melting points and yields are presented in Table 1.

1-Aryl-4-hydrazinecarbonyl-2-pyrrolidinones 2a-c. A solution of the corresponding esters **1a-c** (0.2 mol), hydrazine hydrate, (30.04 g, 0.6 mol) and 2-propanol (30 ml) was refluxed for 1 h. The reaction mixture was cooled and the precipitate was filtered and washed with 2-propanol and diethyl ether.

Compound 2a. IR spectrum, ν, cm^{-1}: 3313.76 (NH_2); 3282.02 (NH); 1683.50 (C=O); 1637.47 (C=O); 782.69-649.15 (Ar). Mass-spectrum, *m/z*: 234.4 $[M]^+$.

Compound 2b. IR spectrum, ν, cm^{-1}: 3311.28 (NH_2); 3281.56 (NH); 1681.07 (C=O); 1637.08 (C=O); 822.36-650.77 (Ar). Mass-spectrum, *m/z*: 234.4 $[M]^+$.

Compound 2c. IR spectrum, ν, cm^{-1}: 3325.58 (NH_2, NH); 1678.09 (C=O); 1630.80 (C=O); 808.68-647.92 (Ar). Mass-spectrum, *m/z*: 248.4 $[M]^+$.

1-Aryl-4-isopropylidenhydrazinecarbonyl-2-pyrrolidinones 3a-c. A solution of the corresponding hydrazides **2a-c** (4.3 mmol) and acetone (30 ml) was refluxed for 3 h. The reaction mixture was cooled and the precipitate was filtered and washed with diethyl ether.

Compound 3a. IR spectrum, ν, cm^{-1}: 3213.18 (NH); 1698.54 (C=O); 1682.95 (C=O); 784.57-664.58 (Ar). Mass-spectrum, *m/z*: 274.4 $[M]^+$.

Compound 3b. IR spectrum, ν, cm^{-1}: 3190.66 (NH); 1701.57 (C=O); 1674.91 (C=O); 825.91-658.3 (Ar). Mass-spectrum, *m/z*: 274.4 $[M]^+$.

Compound 3c. IR spectrum, ν, cm^{-1}: 3205.12 (NH), 1705.36 (C=O); 1680.45 (C=O); 865.96-684.97 (Ar). Mass-spectrum, *m/z*: 288.4 $[M]^+$.

1-Aryl-4-[(3,5-dimethylpyrazol-1-yl)carbonyl]-2-pyrrolidinones 4a-c. A solution of the corresponding hydrazides **2a-c** (13 mmol) and 2,4-pentandione (3.86 g, 39 mmol) and 2-propanol (50 ml) in the presence of catalytic amount of hydrochloric acid was refluxed for 2 h. The solvent was evaporated. The product precipitated from water. The precipitate was filtered and washed with water.

Compound 4a. IR spectrum, ν, cm^{-1}: 1727.13 (C=O); 1698.67 (C=O); 845.65-687.93 (Ar). Mass-spectrum, *m/z*: 298.4 $[M]^+$.

Compound 4b. IR spectrum, ν, cm^{-1}: 1731.92 (C=O); 1701.47 (C=O); 822.56-708.64 (Ar). Mass-spectrum, *m/z*: 298.4 $[M]^+$.

Compound 4c. IR spectrum, ν, cm^{-1}: 1721.54 (C=O); 1698.73 (C=O); 843.18-698.69 (Ar). Mass-spectrum, *m/z*: 312.4 $[M]^+$.

1-Aryl-4-arylidenhydrazinecarbonyl-2-pyrrolidinones 5-9. A solution of hydrazide **2b** (3.02 g, 13 mmol), the corresponding aldehyde (19 mmol), in ethanol (30 ml) was refluxed for 2 h. The reaction mixture was cooled and the precipitate was filtered and washed with ethanol and diethyl ether.

Compound 5. IR spectrum, ν, cm^{-1}: 3263.13 (NH); 1663.86 (C=O, C=O); 852.96-670.52 (Ar). Mass-spectrum, *m/z*: 400 $[M]^+$.

Compound 6. IR spectrum, ν, cm^{-1}: 3124.4 (NH); 1691.03 (C=O); 1656.09 (C=O); 1530.49 (NO_2); 856.12-687.90 (Ar). Mass-spectrum, *m/z*: 367.3 $[M]^+$.

Compound 7. IR spectrum, ν, cm^{-1}: 3292.14 (NH, OH); 1677.32 (C=O); 1635.72 (C=O); 836.53-683.36 (Ar). Mass-spectrum, *m/z*: 338.3 $[M]^+$.

Compound 8. IR spectrum, ν, cm^{-1}: 3226.82 (NH); 1673.81 (C=O); 1611.93 (C=O); 845.37-689.05 (Ar). Mass-spectrum, *m/z*: 365.4 $[M]^+$.

Compound 9. IR spectrum, ν, cm^{-1}: 3013.71 (NH); 1686.65 (C=O); 1665.50 (C=O); 805.77-683.19 (Ar). Mass-spectrum, *m/z*: 439.3 $[M]^+$, 365.4.

1-Aryl-4-[(2-arylidene-1-ethylhydrazine)carbonyl]-2-pyrrolidinones 10-12. A solution of the corresponding hydrazide **5, 6, 8** (27 mmol) and ethyl iodide (50 ml) in the presence of KOH (81 mmol) and K_2CO_3 (81 mmol) was stirred at 50°C for 4 h. The reaction mixture was diluted with acetone (50 ml), and the inorganic compounds were filtered off. The solvent was evaporated under reduced pressure. The product precipitated from water, and the precipitate was filtered and washed with water.

Compound 10. IR spectrum, ν, cm^{-1}: 1693.22 (C=O); 1673.49 (C=O); 1613.25 (NO_2); 846.62-679.03 (Ar). Mass-spectrum, *m/z*: 395.3 $[M]^+$.

Compound 11. IR spectrum, ν, cm^{-1}: 1673.44 (C=O, C=O); 816.25-671.31 (Ar). Mass-spectrum, *m/z*: 428 $[M]^+$.

Compound 12. IR spectrum, ν, cm^{-1}: 1698.10 (C=O); 1663.18 (C=O); 833.01-674.37 (Ar). Mass-spectrum, *m/z*: 393.4 $[M]^+$.

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