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SYNTHESIS AND PROPERTIES OF METHYL HYDROPYRIMIDINEACETATES

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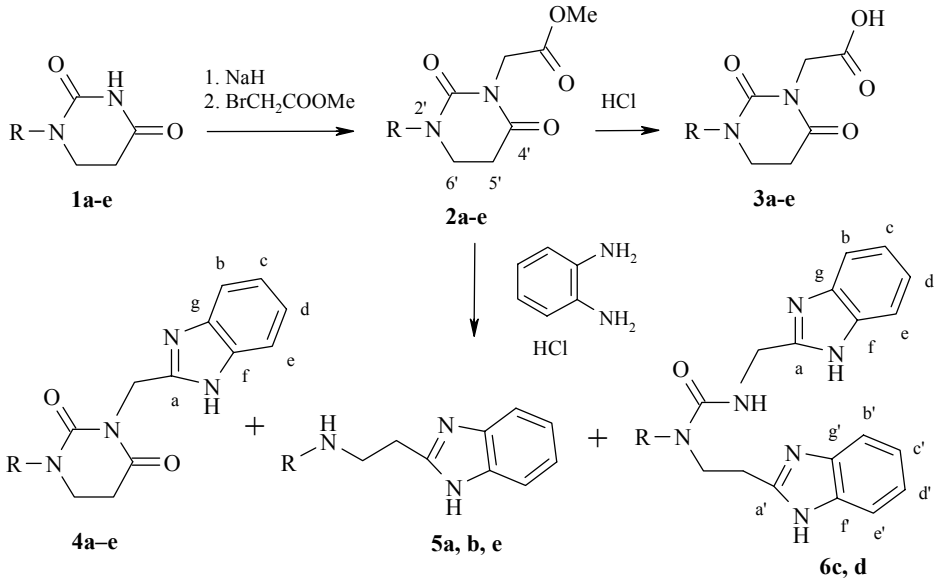
The alkylation of 1-aryl-substituted dihydro-2,4(1H,3H)-pyrimidinediones with methyl 2-bromoacetate has been studied followed by hydrolysis and condensation of the products with o-phenylenediamine. The compounds have been identified by NMR, and IR spectrometry and mass spectrometry. Structural characteristics in the ^{1}H and ^{13}C NMR spectra of the synthesized are discussed.

Keywords: 1-aryldihydro-2,4(1H,3H)-pyrimidinedione, benzimidazoles, hydropyrimidineacetic acids, alkylation, condensation, NMR, IR, mass spectrometry.

Pyrimidineacetic acids and their derivatives possess biological activity [1-4]. However there is no information on the synthesis of dihydropyrimidineacetic acids. The objective of our work was the synthesis and investigation of some chemical properties of the products of alkylation of 1-aryl-substituted dihydro-2,4-(1H,3H)-pyrimidinediones with methyl bromoacetate.

Scheme 1



a R = Ph, **b** R = 4-MeC_6H_4, **c** R = 2,4-$Me_2C_6H_3$, **d** R = 2-Me-5-ClC_6H_3, **e** R = 4-Me-3-ClC_6H_3

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Table 1. Characteristics of the Compounds Synthesized.

Compound	Empirical formula	Found, % / Calculated, %			R_f*	mp, °C*[2]	Yield, %
		C	H	N			
2a	$C_{13}H_{14}N_2O_4$	59.54 / 59.16	5.38 / 5.46	10.68 / 10.34		110-111	40
2b	$C_{14}H_{16}N_2O_4$	60.86 / 60.66	5.84 / 5.48	10.14 / 10.39		108-109	55
2c	$C_{15}H_{18}N_2O_4$	62.06 / 62.43	6.25 / 5.99	9.65 / 9.58		120-121	30
2d	$C_{14}H_{15}ClN_2O_4$	54.11 / 53.89	4.87 / 4.63	9.02 / 8.96		97-98	66
2e	$C_{14}H_{15}ClN_2O_4$	54.11 / 54.35	4.87 / 4.53	9.02 / 9.31		101-102	92
3a	$C_{12}H_{12}N_2O_4$	58.06 / 58.21	4.87 / 4.75	11.29 / 11.13		149-150	38
3b	$C_{13}H_{14}N_2O_4$	59.54 / 59.21	5.38 / 5.03	10.68 / 10.57		202-203	72
3c	$C_{14}H_{16}N_2O_4$	60.86 / 60.57	5.84 / 5.49	10.14 / 10.32		165 (dec.)	51
3d	$C_{13}H_{13}ClN_2O_4$	52.62 / 52.23	4.42 / 4.34	9.44 / 9.28		184-185	56
3e	$C_{13}H_{13}ClN_2O_4$	52.62 / 52.37	4.42 / 4.17	9.44 / 9.31		143-144	64
4a	$C_{18}H_{16}N_4O_2$	67.49 / 67.62	5.03 / 5.36	17.49 / 17.55	0.41	230 (dec.)	21
4b	$C_{19}H_{18}N_4O_2$	68.25 / 68.59	5.43 / 5.46	16.76 / 16.49	0.46	245-246	43
4c	$C_{20}H_{20}N_4O_2$	68.95 / 68.88	5.79 / 5.43	16.08 / 16.30	0.55	193-194	38
4d	$C_{19}H_{17}ClN_4O_2$	61.88 / 61.55	4.65 / 4.36	15.19 / 15.11	0.59	128-129	42
4e	$C_{19}H_{17}ClN_4O_2$	61.88 / 61.73	4.65 / 4.60	15.19 / 15.36	0.52	159 (dec.)	30
5a	$C_{15}H_{15}N_3$	75.92 / 75.82	6.37 / 6.30	17.71 / 17.56	0.64	Resin	11
5b	$C_{16}H_{17}N_3$	76.46 / 76.63	6.82 / 6.56	16.72 / 16.59	0.62	Resin	11
5e	$C_{16}H_{16}ClN_3$	67.25 / 67.33	5.64 / 5.43	14.70 / 14.89	0.73	145 (dec.)	14
6c	$C_{26}H_{26}N_6O$	71.43 / 71.21	6.18 / 5.98	19.27 / 19.16	0.23	151-152	23
6d	$C_{25}H_{23}ClN_6O$	65.48 / 65.43	5.35 / 5.05	18.03 / 18.31	0.2	149-150	24

* Acetone–hexane, 1:1

*[2] Solvents: toluene (compounds **2a,b,d**,**e**) and 2-propanol (compound **2c**).

We have established that the reaction of 1-aryl-substituted dihydro-2,4(1H,3H)-pyrimidinediones **1a-e** with methyl bromoacetate in DMF in the presence of sodium hydroxide occurred uniquely to give the products of N-alkylation – methyl 2-[3-aryl-2,6-dioxohexahydro-1-pyrimidyl]acetates **2a-e,** separated from the reaction mixture by dilution with water and ice. The dihydropyrimidineacetic acids **3a-e** were prepared by boiling the corresponding esters **2a-e** in 10% hydrochloric acid with subsequent cooling of the reaction mixture to 4°C.

The possibility of synthesis of benzimidazole system by the Phillips method from the carboxylic acids and *o*-phenylenediamine was explored. On investigating the products of the condensation of the methyl esters **2a-e** with *o*-phenylenediamine in 4M hydrochloric acid it appeared that two products were formed in each reaction – 1-aryl-3-(1H-benzimidazolylmethyl)dihydropyrimidine-2,4(1H,3H)-diones **4a-e** and products of the decompo-sition of the hydropyrimidine ring – N-aryl-N-[2-(1H-benzimidazol-2-yl]amines **5a,b,e,** or N-[2-(1H)-benzimidazol-2-yl)ethyl]-N′-(1H-benzimidazol-2-yl)-disubstituted phenylureas **6c,d** (Table 1). It is probable

TABLE 2. Spectral Characteristics of the Compounds Synthesized

Compound	IR spectrum, ν, cm^{-1}	^1H NMR, δ, ppm (*J*, Hz)*	Mass spectrum, *m/z* ($I_{отн}$, %)
1	2	3	4
2a	1673, 1719, 1754 (C=O)	2.95 (2H, t, *J* = 6.6, CH_2CO); 3.69 (3H, s, $COOCH_3$); 3.91 (2H, t, *J* = 6.6, CH_2N); 4.48 (2H, s, NCH_2CO); 7.22-7.44 (5H, m, H arom.)	263 $[M+H]^+$ (100)
2b	1667, 1720, 1752 (C=O)	2.33 (3H, s, 4-CH_3); 2.93 (2H, t, *J* = 6.6, CH_2CO); 3.69 (3H, s, $COOCH_3$); 3.90 (2H, t, *J* = 6.6, CH_2N); 4.47 (2H, s, NCH_2CO); 7.19-7.27 (4H, m, H arom.)	277 $[M+H]^+$ (100)
2c	1669, 1717, 1748 (C=O)	2.20 (3H, s, 2-CH_3); 2.30 (3H, s, 4-CH_3); 2.94 (2H, t, *J* = 6.6, CH_2CO); 3.68 (3H, s, $COOCH_3$); 3.60-3.93 (2H, m, CH_2N); 4.42 (1H, d, *J* = 16.9, NCH_2CO/H_A); 4.52 (1H, d, *J* = 16.9, NCH_2CO/H_B); 7.03-7.16 (3H, m, H arom.)	291 $[M+H]^+$ (100)
2d	1682, 1720, 1748 (C=O)	2.24 (3H, s, 2-CH_3); 2.99 (2H, t, *J* = 6.6, CH_2CO); 3.69 (3H, s, $COOCH_3$); 3.69-3.99 (2H, m, CH_2N); 4.42 (1H, d, *J* = 16.9, NCH_2CO/H_A); 4.52 (1H, d, *J* = 16.9, NCH_2CO/H_B); 7.27-7.39 (3H, m, H arom.)	311 $[M+H]^+$ (100)*[2]
2e	1667, 1723, 1756 (C=O)	2.31 (3H, s, 4-CH_3); 2.90 (2H, t, *J* = 6.6, CH_2CO); 3.64 (3H, s, $COOCH_3$); 3.80 (2H, t, *J* = 6.6, CH_2N); 4.41 (2H, s, NCH_2CO); 7.20-7.44 (3H, m, H arom.)	311 $[M+H]^+$ (100)*[2]
3a	1660, 1704, 1767 (C=O)	2.95 (2H, t, *J* = 6.6, CH_2CO); 3.95 (2H, t, *J* = 6.6, CH_2N); 4.48 (2H, s, NCH_2CO); 7.22-7.44 (5H, m, H arom.); 11.28 (1H, br. s, COOH)	249 $[M+H]^+$ (100)
3b	1644, 1698, 1768 (C=O)	2.32 (3H, s, 4-CH_3); 2.93 (2H, t, *J* = 6.6, CH_2CO); 3.90 (2H, t, *J* = 6.6, CH_2N); 4.47 (2H, s, NCH_2CO); 7.18-7.24 (4H, m, H arom.); 11.26 (1H, br. s, COOH)	263 $[M+H]^+$ (100)
3c	1661, 1710, 1749 (C=O)	2.20 (3H, s, 2-CH_3); 2.30 (3H, s, 4-CH_3); 2.94 (2H, t, *J* = 6.6, CH_2CO); 3.63-3.91 (2H, m, CH_2N); 4.43 (1H, d, *J* = 17.0, NCH_2CO/H_A); 4.52 (1H, d, *J* = 17.0, NCH_2CO/H_B); 7.03-7.15 (3H, m, H arom.); 11.26 (1H, br. s, COOH)	277 $[M+H]^+$ (100)
3d	1681, 1724, 1730 (C=O)	2.24 (3H, s, 2-CH_3); 2.99 (2H, t, *J* = 6.7, CH_2CO); 3.70-4.01 (2H, m, CH_2N); 4.43 (1H, d, *J* = 17.0, NCH_2CO/H_A); 4.53 (1H, d, *J* = 17.0, NCH_2CO/H_B); 7.27-7.41 (3H, m, H arom.); 10.99 (1H, br. s, COOH)	297 $[M+H]^+$ (100)*[2]
3e	1662, 1708, 1750 (C=O)	2.33 (3H, s, 4-CH_3); 2.90 (2H, t, *J* = 6.7, CH_2CO); 3.81 (2H, t, *J* = 6.7, CH_2N); 4.43 (1H, s, NCH_2CO); 7.22-7.45 (3H, m, H arom.); 7.81 (1H, br. s, COOH)	297 $[M+H]^+$ (100)*[2]

TABLE 2.(continued)

1	2	3	4
4a	1677, 1723 (C=O); 2643, 2852, 2916 (NH)	2.95 (2H, t, *J* = 6.6, CH_2CO); 3.90 (2H, t, *J* = 6.6, CH_2N); 5.10 (2H, s, NCH_2C=); 7.12-7.55 (9H, m, H arom.); 12.24 (1H, s, NH)	321 $[M+H]^+$ (100)
4b	1671, 1721 (C=O); 2920, 3030, 3055 (NH)	2.30 (3H, s, 4-CH_3);2.95 (2H, t, *J* = 6.7, CH_2CO); 3.86 (2H, t, *J* = 6.7, CH_2N); 5.08 (2H, s, NCH_2C=); 7.11-7.61 (8H, m, H arom.); 12.22 (1H, s, NH)	335 $[M+H]^+$ (100)
4c	1675, 1721 (C=O); 2764, 2923, 3071 (NH)	2.14 (3H, s, 2-CH_3); 2.27 (3H, s, 4-CH_3); 2.98 (2H, t, *J* = 6.7, CH_2CO); 3.59-3.83 (2H, m, CH_2N); 5.07 (1H, d, *J* = 16.0, NCH_2C=/H_A); 5.16 (1H, d, *J* = 16.0, NCH_2C=/H_B); 7.03-7.52 (7H, m, H arom.); 12.18 (1H, br. s, NH)	349 $[M+H]^+$ (100)
4d	1673, 1719 (C=O); 2739, 2854, 2922 (NH)	2.17 (3H, s, 2-CH_3); 3.00 (2H, t, *J* = 6.7, CH_2CO); 3.63-3.83 (2H, m, CH_2N); 5.03 (1H, d, *J* = 15.9, NCH_2C=/H_A); 5.15 (1H, d, *J* = 15.9, NCH_2C=/H_B); 7.11-7.53 (7H, m, H arom.); 7.11 (1H, m, NH); 12.23 (1H, br. s, NH)	369 $[M+H]^+$ (100)*[2]
4e	1666, 1727 (C=O); 2753, 2852, 2919 (NH)	2.32 (3H, s, 4-CH_3); 2.96 (2H, t, *J* = 6.7, CH_2CO); 3.89 (2H, t, *J* = 6.7, CH_2N); 5.08 (2H, s, NCH_2C=); 7.11-7.55 (7H, m, H arom.), 12.25 (1H, s, NH)	369 $[M+H]^+$ (100)*[2]
5a		3.06 (2H, t, *J* = 7.3, CH_2(C=)); 3.45-3.62 (2H, m, $NHCH_2$); 5.73 (2H, t, *J* = 5.8, CH_2NH); 6.51-7.52 (9H, m, H arom.), 12.27 (1H, s, NH)	238 $[M+H]^+$ (100)
5b		2.15 (3H, s, 4-CH_3); 3.05 (2H, t, *J* = 7.3, CH_2(C=)); 3.46 (2H, t, *J* = 7.3, CH_2NH); 5.49 (1H, br. s, CH_2NH); 6.53-7.48 (8H, m, H arom.); 12.22 (1H, s, NH)	252 $[M+H]^+$ (100)
5e		2.16 (3H, s, 2-CH_3); 3.04 (2H, t, *J* = 7.2, CH_2(C=)); 3.44-3.51 (2H, m, $NHCH_2$); 5.90 (1H, t, *J* = 5.8, CH_2NH); 6.50-7.50 (7H, m, H arom.); 12.27 (1H, s, NH)	286 $[M+H]^+$ (100)*[2]
6c		2.14 (3H, s, 2-CH_3); 2.28 (3H, s, 4-CH_3); 3.05 (2H, t, *J* = 7.7, CH_2CH_2(C=)); 3.69, 4.23 (2H, 2br. s, NCH_2); 4.42 (2H, d, *J* = 5.6, CH_2NH); 6.18 (1H, s, CH_2NH); 7.01-7.52 (11H, m, H arom.); 11.84 (2H, 2br. s, NH)	439 $[M+H]^+$ (100)
6d		2.14 (3H, s, 2-CH_3); 3.09 (2H, t, *J* = 7.5, CH_2CH_2C=); 3.74, 4.18 (2H, 2 br. s, NCH_2); 4.42 (2H, d, *J* = 5.6, CH_2NH); 6.59 (1H, br. s, CH_2NH); 7.08-7.51 (11H, m, H arom.); 12.18 (2H, s, NH)	459 $[M+H]^+$ (100)*[2]

* ^{1}H NMR spectra were recorded in acetone-d_6 (compounds **2a-e**) and DMSO-d_6 (compounds **4-6**).

*[2] The cited $[M + H]^+$ contain the isotope ^{35}Cl.

that the reaction occurs in two directions. The first direction is the condensation of *o*-phenylenediamine with the esters **2** to give compounds **4a-e**. The second direction of the reaction is that the nucleophile diamine attacks the 4-CO group of the heterocycle with subsequent opening of the heterocycle to form the benzimidazole fragment (compounds **6c,d**) with subsequent hydrolysis of the amide to give compounds with the structures **5a,b,e**.

The structures of the compounds synthesized were confirmed by IR, mass spectrometry, and ^{1}H and ^{13}C NMR spectroscopy (Table 2) with assignment of the signals on the basis of general rules of additivity of substituents and published spectral data of model compounds [5-9].

With the necessity to assign spectral lines we used the APT ^{13}C NMR method [5, 6]. The investigation compounds are divided to for classes according the characteristic features of their structural fragments. The substituent R in all the compounds synthesized has the form of a benzene ring with varying degrees of substitution. The spectral lines of the carbon atoms of the benzene ring for compounds **2a-e** and **4a-e** in their ^{13}H NMR spectra were identified on the basis of the refined in the given word increments (C_i = 12.05, C_o = -1.32, C_m = 2.06, and C_p = -0.54 ppm) of the influence of the substituent in the pyrimidine ring [8], in the case of compounds **5a,b,e** the refined influence of the fragment $NHCH_2CH_2$ [5-7] (C_i = 19.97, C_o = -16.41, C_m = 0.43, and C_p = -12.69 ppm), but in compounds **6c-d** by comparison with related fragments in model compounds [9]. The character of the substitution on the benzene ring has an important effect on the structural characteristics and properties of the compound. With no substituent on the benzene ring (compounds **2a-5a**) or with *p*- or *m*-substituents (compounds **2b-5b** and **2e-5e**) the aliphatic hydrogen atoms appear in the ^{1}H NMR spectra as triplets (Table 3, Fig., **4b**), while hydrogen atoms of the $NCH_2C=$ fragment are observed as a sharp singlet. Substituent in the *o*-position (compounds **2c-4c, 2d-4d**) hinder rotation about the C(1)-N bond, as a consequence of which the hydrogen atoms in the NCH_2 fragment appear as an AB spin-spin multiplet in the ABX_2 spin-spin system (Fig., **4c**). The hydrogen atoms in the $NCH_2C=$ fragment appear as an AB spin-spin multiplet. In the ^{13} C NMR spectra of compounds with an *o*-substituent in the benzene ring, no specific changes in the chemical shifts of the carbon atoms of the pyrimidinedione ring were observed.

Table 3. ^{13}C NMR Spectral Data for Compounds **2a-d**

Carbon atoms	Chemical shifts (acetone-d_6), δ, ppm			
	2a	**2b**	**2c**	**2d**
C-1	144.55	142.04	140.78	144.38
C-2	127.18	127.11	137.28	136.90
C-3	130.56	131.08	133.17	133.93
C-4	127.96	137.67	139.14	129.02 or 129.48
C-5	130.56	131.08	128.63 or 129.24	132.93
C-6	127.18	127.11	128.63 or 129.24	129.02 or 129.48
C-2'	154.13	154.14	153.67	153.63
C-4'	170.59 or 170.85	170.61 or 170.80	170.66 or 170.99	170.56 or 170.87
C-5'	33.21	33.23	33.32	33.24
C-6'	45.78	45.90	45.76	45.54
$N\underline{C}H_2COO$	43.12	43.11	43.01	43.02
$CH_2\underline{C}OO$	170.59 or 170.85	170.61 or 170.80	170.66 or 170.99	170.56 or 170.87
OCH_3	53.31	53.29	53.28	53.33
2-CH_3			18.83	18.45
4-CH_3		21.92	21.96	

The characteristics of the ^{1}H NMR spectra of compounds **2a-e** are the singlet for the $COOCH_3$ group at 3.6 ppm and correspondingly in the ^{13}C NMR spectra carbon resonances at 170 and 53 ppm. The structures of compounds **3a-e** were confirmed by the broad singlet at 11.3 ppm in the ^{1}H NMR spectra. The presence of the characteristic benzimidazole multiplets in the aromatic proton region [10-12] and a broad singlet at 12.2 ppm in the ^{1}H NMR spectrum indicate the formation of compounds of type **4a-e**. In the ^{13}C NMR spectra the presence

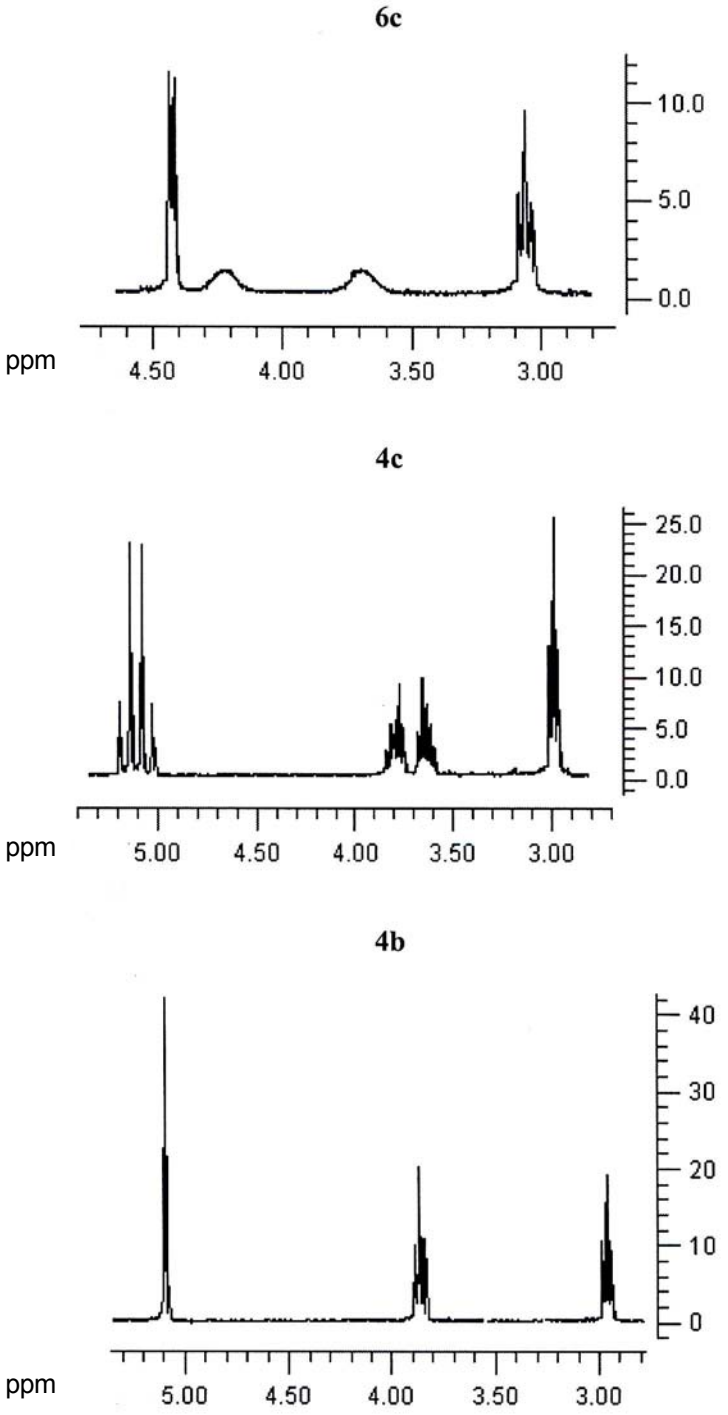

Fig. Aliphatic proton parts of the ^{1}H NMR spectra of compounds **4b**,**c** and **6c.**

of the benzimidazole fragment is confirmed by a group of lines characteristically broadened because of exchange processes - the lines are sometimes lost in the background (compounds **4b,c**) and also a signal at 150 ppm, assigned to the atom C-a.

It is characteristic of compounds **5a,b,e,** products of decomposition of the hydropyrimidine ring, that a second signal for NH at 5.5 ppm in the ^{1}H NMR spectrum appears, sometimes observed as a triplet because of spin-spin interaction with the protons of the CH_2 group, and the presence of the CH_2CH_2, fragment in which the difference of chemical shifts is 0.5 ppm less than in the corresponding fragment of the pyrimidinedione ring, and the absence of the lines of the carbon in the carbonyl groups at 150 and 169 ppm in the ^{13}C NMR spectrum.

On decomposition of the hydropyrimidine ring in compounds with *o*-substitution in the benzene ring, stable compounds **6c,d** are formed in which there are two benzimidazole units. The structures of compounds **6c,d** are confirmed by the presence of two broad singlets of the NH of the benzimidazole fragments at 12.2 and the singlet of the NH group at 6.2 ppm in the ^{1}H NMR spectra. The presence of a doublet at 4.4 ppm indicates the existence of the $NHCH_2C=$ unit. The presence of a fast exchange process of molecules of compounds in the solutions **6c,d** is indicated by the broad the multiplets of the fragment $NCH_2CH_2C=$ (Fig. **6c**), while in the absence of exchange a resolution of the multiplets is observed (Fig. **4c,b**). Careful integration of the ^{1}H NMR spectra of compounds **6c,d** confirmed the presence of the required number of protons and the fragments mentioned above.

Table 4. ^{13}C NMR Spectral Data for Compounds **4a-e**

Carbon atoms	Chemical shifts (DMSO-d_6), δ, ppm				
	4a	**4b**	**4c**	**4d**	**4e**
C-1	142.33	139.82	138.59	142.23	141.26
C-2	125.21	125.11	135.04	134.79	125.68
C-3	128.67	129.12	131.16	132.14	132.76 or 133.16
C-4	126.00	135.32	136.85	127.29 or 127.54	132.76 or 133.16
C-5	128.67	129.12	126.95 or 127.29	130.31	131.08
C-6	125.21	125.11	126.95 or 127.29	127.29 or 127.54	123.87
C-2'	151.04 or 152.24	151.07 or 152.23	151.09 or 151.78	150.96 or 151.79	150.99 or 152.26
C-4'	169.50	169.53	169.64	169.57	169.49
C-5'	31.33	31.33	31.44	31.35	31.26
C-6'	43.55	43.65	43.58	43.34	43.51
$N\underline{CH_2}C=$	38.44	38.42	38.23	38.28	38.52
C-a	151.04 or 152.24	151.07 or 152.23	151.09 or 151.78	150.96 or 151.79	150.99 or 152.26
C-b	118.36	Not observed	114.69	118.30	118.33
C-c	121.10 or 121.68	121.36	121.40	121.10 or 121.83	121.16 or 121.78
C-d	121.10 or 121.68	121.36	121.40	121.10 or 121.83	121.16 or 121.78
C-e	111.04	Not observed	111.15	111.09	111.11
C-f	134.16	Not observed	Not observed	134.20	134.26
C-g	143.04	Not observed.	Not observed	143.05	143.22
2-CH_3			17.32	16.91	
4-CH_3		20.50	20.54		19.11

The presence of lines at 156, 153, an 152 ppm in the ^{13}C NMR spectra of compounds **6c,d** indicates the existence of the NCONH fragment, and correspondingly the C-a and C′-a atoms of the benzimidazole unit. The lines at 47, 27, and 38 ppm are unambiguously assigned to the carbon atoms of the fragments $N\underline{CH_2}CH_2$, $NCH_2\underline{CH_2}$, and $CONH\underline{CH_2}C=$ respectively.

For comparison (Tables 3 and 4) of the chemical shifts of the corresponding fragments of compounds **2a-e** and **4a-e** it should be noted that in the spectra of compounds **2a-e**, recorded in acetone-d_6, a weak field shift of the lines of the aliphatic and aromatic carbon atoms by 2 ppm was observed in the ^{13}C NMR spectra.

Table 5. ^{13}C NMR Spectral Data for Compounds **5a,b,c**

Carbon atoms	Chemical shifts (DMSO-d_6), δ, ppm		
	5a	**5b**	**5e**
C-1	148.47	146.22	147.99
C-2	112.09	112.28	111.29 or 111.80
C-3	128.93	129.37	133.64
C-4	115.81	124.20	121.44
C-5	128.93	129.37	131.39
C-6	112.09	112.28	111.29 or 111.80
$NH\underline{CH_2}CH_2$	41.41	41.72	41.39
$NHCH_2\underline{CH_2}$	28.58	28.61	28.50
C-a	153.16	153.22	153.05
C-b	118.12	118.29	118.20
C-c	121.39 or 121.44	121.15 or 121.29	121.01 or 121.10
C-d	121.39 or 121.44	121.15 or 121.29	121.01 or 121.10
C-e	110.73	110.83	110.54
C-f	134.21	134.45	134.32
C-g	143.31	142.41	143.18
2-CH_3			
4-CH_3		20.05	18.46

Table 6. ^{13}C NMR Spectral Data for Compounds **6c,d**

Carbon atoms	Chemical shifts (DMSO-d_6), δ, ppm.	
	6c	**6d**
C-1	137.11 or 137.26	141.54
C-2	137.11 or 137.26	135.90
C-3	131.94	130.58
C-4	136.37	129.41
C-5	127.73	127.67
C-6	129.36	132.60
NCONH	156.65	156.32
$NH\underline{CH_2}C=$	38.75	38.28
$N\underline{CH_2}CH_2C=$	47.25	47.44
$NCH_2\underline{CH_2}C=$	27.88	27.88
C-a / C-a'	152.48 or 153.40	152.44 or 153.41
C-b / C-b'	114.69 or 114.80	118.33 or 118.42
C-c / C-c'	121.25 or 121.32	121.30 or 121.37
C-d / C-d'	121.25 or 121.32	121.30 or 121.37
C-e/ C-e'	114.69 or 114.80	110.75 or 110.83
C-f / C-f'	138.87	134.23 or 134.56
C-g / C-g'	138.87	143.33 or 143.63
2-CH_3	17.26	16.91
4-CH_3	20.60	

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded with TMS as internal standard on a Varian Unity Inova (300 and 75 MHz respectively) spectrometer. IR spectra of KBr disks were recorded on a Perkin-Elmer Bx FT-IR instrument. Mass spectra were recorded on a Waters ZQ 2000 instrument, with 15 eV ionizing voltage. Monitoring of the course of reaction and purity of the compounds synthesized was *via* TLC using Silufol UV-254, with development with UV light or iodine vapor.

Methyl [3-aryl-2,6-dioxotetrarylpyrimidin-1-(2H)-yl]acetates (2a-e) (General Method). A 60% suspension of sodium hydroxide in paraffin (2.40 g, 60 mmol) was added to dry DMF (100 ml) with stirring. The corresponding 1-aryldihydro-2,4-pyrimidinedione **1a-e** (50 mmol) dissolved in dry DMF (50 ml) was added to the suspension in 10 min with stirring. The mixture was maintained at 50°C and stirring was continued until evolution of hydrogen ceased (~45 min). The mixture was cooled to 5-10°C, 2-bromomethyl acetate (14.2 ml, 150 mmol), dissolved in dry DMF (20 ml), was added dropwise over 10 min. The temperature of the mixture was increased to 50-60°C, stirring was continued for 30 min, the mixture was cooled to 20°C and the mixture was poured into a mixture of ice and water (~500 ml). The crystals of compounds **2a-e** were filtered off, washed with water, dried and recrystallized from the relevant solvent.

[3-Aryl-2,6-dioxohexahydropyrimidin-1-(2H)-yl]acetic Acids 3a-e (General Method). A solution of 2 mmol of the corresponding ester **2a-e** in 10% hydrochloric acid (12 ml) was boiled for 2 h, cooled, and the precipitated compound **3a-e** was filtered off, washed with water, and dried. The solid was twice dissolved in 5% Na_2CO_3 solution, filtered, and precipitated with 5% hydrochloric acid.

3-(1H-Benzimidazol-2-ylmethyl)-1-aryldihydropyrimidine-2,4(1H,3H)-diones 4a-e, N-aryl-N-[2-(1H-benzimidazol-2-yl)ethyl]amines, 5a,b,e, and N-arylN-[2-(1H-benzimidazol-2-yl)ethyl]-N′-(1H-benzimidazol-2-ylmethyl)urea, 6c,d (General Method). A solution of 4 mmol of the corresponding ester **2a-e** and *o*-phenylenediamine (1.30 g, 12 mmol) in 4M hydrochloric acid (12 ml) was boiled for 16 h, cooled, and neutralized 25% ammonia to pH 8-9. The precipitate was filtered off and purified by column chromatography with 1:1 acetone–hexane as eluent.

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