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Azines and Azoles: CXXVI.[1] First Example of a Novel Heterocyclic System: Pyrimido[1,6-*a*][1,5]benzodiazepines

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Abstract—4-Hydroxy-5-(2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-2*H*-1,3-thiazine-2,6-diones readily undergo acylation at the N^1 atom of the benzodiazepine system by the action of acetic anhydride. Heating of the acetylated products in boiling dimethylformamide leads to the formation of 75–93% of the corresponding 7-acetyl-6-R-6,7-dihydropyrimido[1,6-*a*][1,5]benzodiazepine-1,3-diones that are derivatives of hitherto unknown fused heterocyclic system, pyrimido[1,6-*a*][1,5]benzodiazepine. 4-Hydroxy-5-(2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-2*H*-1,3-thiazine-2,6-diones are converted into 1-(2-aminophenyl)-6-(2-R-vinyl)uracils on heating in boiling DMF.

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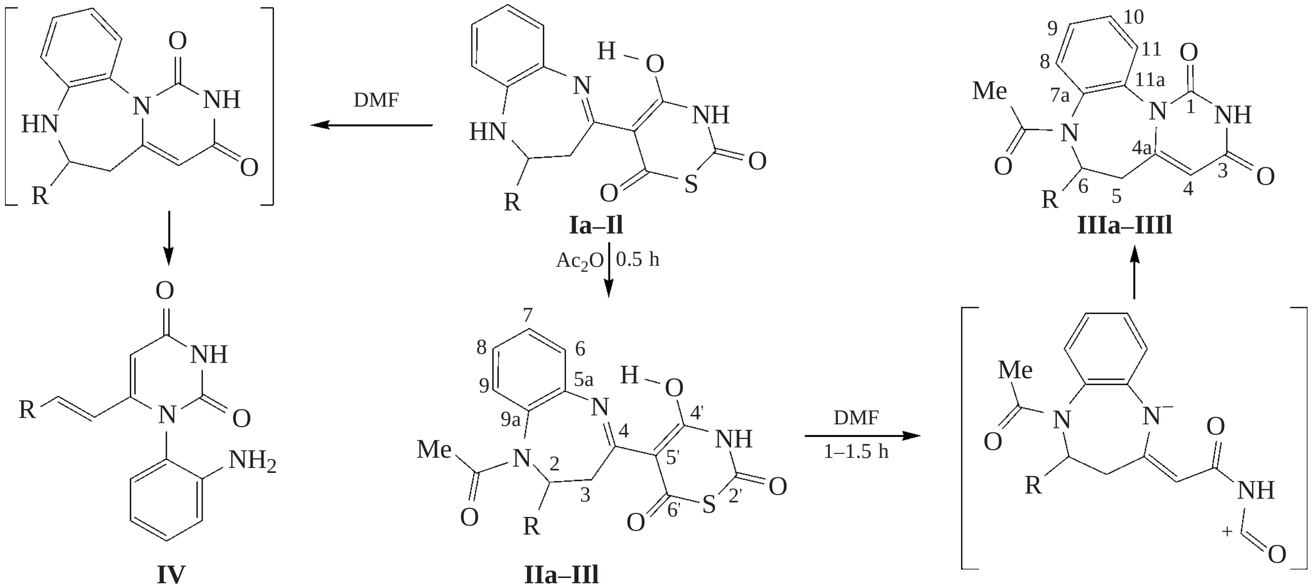
We recently developed a very simple and convenient procedure for the synthesis of 5-acetyl-4-hydroxy-3,6-dihydro-2*H*-1,3-thiazine-2,6-dione from malonic acid, potassium thiocyanate, and acetic anhydride in acetic acid at room temperature [2–4] and found that this compound reacts with *o*-phenylenediamine and 1.5–2 equiv of an aldehyde or ketone in propan-1-ol in the presence of a catalytic amount of trifluoroacetic acid (reaction time 1–1.5 h) to give 2-substituted 2,3-dihydro-1*H*-1,5-benzodiazepines **Ia**–**Il** in good yields [5].

Scheme 1.



I–III, R = Ph (**a**), 4-MeC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**), 4-$Me_2NC_6H_4$ (**d**), 4-ClC_6H_4 (**e**), 4-$AcOC_6H_4$ (**f**), 3,4-$(MeO)_2C_6H_3$ (**g**), 3,4-$(AcO)_2C_6H_3$ (**h**), 2-furyl (**i**), 1*H*-indol-3-yl (**j**), PhCH=CH (**k**), β-piperonyl (**l**).

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[1] For communication CXXV, see [1].

Table 1. Yields, melting points, R_f values, and elemental analyses of 5-(1-acetyl-2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-4-hydroxy-2*H*-1,3-thiazine-2,6-diones **IIa**–**IIl**

Comp. no.	Yield, %	mp, °C	R_f (acetone–hexane, 1 : 1)	Found, %			Formula	Calculated, %		
				C	H	N		C	H	N
IIa	90	263–265	0.27	61.53	4.69	10.27	$C_{21}H_{19}N_3O_4S$	61.60	4.68	10.26
IIb	92	284–286	0.30	62.45	5.01	9.94	$C_{22}H_{21}N_3O_4S$	62.40	5.00	9.92
IIc	89	255–257	0.20	60.16	4.83	9.54	$C_{22}H_{21}N_3O_5S$	60.12	4.82	9.56
IId	93	268–271	0.25	61.01	5.35	12.35	$C_{23}H_{24}N_4O_4S$	61.05	5.35	12.38
IIe	84	276–278	0.31	56.86	4.08	9.48	$C_{21}H_{18}ClN_3O_4S$	56.82	4.09	9.47
IIf	82	251–253	0.29	59.14	4.54	8.97	$C_{23}H_{21}N_3O_6S$	59.09	4.53	8.99
IIg	85	225–227	0.18	58.89	4.95	8.93	$C_{23}H_{23}N_3O_6S$	58.84	4.94	8.95
IIh	78	290–292	0.43	57.21	4.42	8.02	$C_{25}H_{23}N_3O_8S$	57.14	4.41	8.00
IIi	75	246–248	0.25	57.18	4.28	10.51	$C_{19}H_{17}N_3O_5S$	57.13	4.29	10.52
IIj	85	257–258	0.15	61.66	4.49	12.47	$C_{23}H_{20}N_4O_4S$	61.59	4.49	12.49
IIk	88	245–247	0.28	63.48	4.85	9.66	$C_{23}H_{21}N_3O_4S$	63.43	4.86	9.65
IIl	91	234–236	0.22	58.46	3.81	9.32	$C_{22}H_{17}N_3O_6S$	58.53	3.80	9.31

Compounds **Ia**–**Il** turned out to readily react with acetic anhydride (within 30 min under reflux) to afford the corresponding 1-acetyl derivatives **IIa**–**IIl** in excellent yield (Scheme 1). Initially, yellow benzodiazepine **Ia**–**Il** dissolves completely within 5–10 min under reflux, and colorless product begins to crystallize from the solution. The products are poorly soluble even in boiling acetic anhydride. The reactions with benzodiazepines **If** and **Ih** were accompanied by acylation of the phenolic hydroxy groups. By contrast, the indole nitrogen atom in compound **Ij** remained intact under these conditions. Acylated benzodiazepines **II** (except for **IId**) exhibit blue fluorescence upon irradiation with UV light, while the initial compounds show bright yellow fluorescence.

The structure of compounds **IIa**–**IIl** was confirmed by the analytical (Table 1) and spectral data (^{1}H and ^{13}C NMR, UV, IR, and mass spectra). The mass spectra of **IIa**–**IIl** (Table 2) contain the molecular ion peak, a strong peak from the $[M – 43]^+$ ion arising from elimination of CH_3CO from the molecular ion (this ion is often the most abundant in the spectrum), and a peak from the $[M – 60]^+$ ion corresponding to expulsion of carbonyl sulfide molecule. In addition, ion peaks resulting from cleavage of the $C^2–C_{arom}$ bond ($[M – R]^+$) and the bond between the benzodiazepine and thiazine rings ($C^4–C^5$, $[M – 144]^+$; 144 is the weight of the thiazine fragment) were observed.

In the ^{1}H NMR spectra of *N*-acetylbenzodiazepines **IIa**–**IIl** in DMSO-d_6 (Table 3) singlets from protons in the OH (δ 13.80–14.07 ppm) and NH groups (δ 11.65–11.85 ppm) of the thiazine ring were present; these signals were appreciably broadened as compared to the corresponding signals of initial compounds **Ia**–**Il**. Aromatic protons in the fused benzene ring and aryl substituent on C^2 resonated as overlapped multiplets at δ 6.25–7.41 ppm. The $C^2H–C^3H_2$ fragment in the benzodiazepine ring gave rise to an *ABX* system

Table 2. Mass spectra of 5-(1-acetyl-2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-4-hydroxy-2*H*-1,3-thiazine-2,6-diones **IIa**–**IIl**

Comp. no.	*m/z* (I_{rel}, %)
IIa	407 M^+ (31), 364 (20), 348 (33), 332 (7), 320 (10), 316 (6), 304 (23), 289 (13), 288 (12), 287 (15), 274 (56), 261 (24), 249 (5), 245 (7), 242 (6), 233 (20), 232 (17), 231 (18), 221 (24), 219 (24), 195 (51), 158 (8), 144 (7), 143 (5), 130 (16), 129 (16), 119 (22), 103 (24), 92 (20), 77 (26), 65 (21), 51 (12), 43 (100)
IIb	421 M^+ (25), 393 (4), 388 (3), 387 (4), 378 (21), 362 (24), 344 (6), 334 (10), 318 (20), 316 (11), 303 (10), 302 (8), 301 (11), 291 (4), 279 (13), 275 (31), 274 (100), 263 (8), 247 (12), 235 (20), 233 (22), 218 (8), 209 (38), 158 (10), 144 (9), 130 (14), 129 (15), 119 (18), 118 (20), 117 (18), 115 (16), 105 (20), 103 (21), 91 (22), 77 (19), 65 (20), 60 (7), 51 (8), 43 (73)

Table 2. (Contd.)

Comp. no.	*m/z* (I_{rel}, %)
IIc	437 M^+ (7), 394 (5), 378 (4), 350 (6), 334 (5), 317 (3), 295 (6), 291 (5), 274 (12), 263 (3), 251 (5), 249 (5), 225 (10), 144 (3),134 (19), 121 (100), 103 (5), 91 (6), 77 (6), 65 (5), 43 (31)
IId	450 M^+ (44), 407 (3), 390 (3), 347 (5), 330 (4), 308 (7), 304 (6), 276 (2), 264 (6), 248 (3), 238 (6), 222 (3), 147 (38), 134 (100), 121 (9), 103 (7), 90 (4), 77 (6), 65 (5), 60 (4), 43 (25)
IIe	443 M^+ (10), 442 (M^+, 6), 441 (M^+, 21), 400 (6), 399 (4), 398 (13), 382 (20), 366 (6), 356 (5), 354 (5), 338 (9), 323 (8), 316 (7), 229 (34), 218 (8), 158 (10), 143 (5), 130 (6), 119 (10), 103 (8), 102 (8), 92 (6), 90 (5), 77 (8), 65 (7), 43 (100)
IIf	465 M^+ (12), 422 (6), 406 (11), 405 (13), 388 (4), 380 (10), 363 (15), 362 (14), 346 (6), 320 (27), 317 (5), 304 (5), 292 (3), 277 (14), 274 (41), 261 (5), 253 (4), 249 (5), 237 (5), 235 (7), 228 (3), 211 (12), 210 (6), 201 (5), 171 (3), 158 (8), 144 (4), 143 (4), 130 (7), 118 (14), 119 (14), 107 (9), 103 (8), 91 (7), 77 (8), 65 (7), 60 (18), 43 (100)
IIg	467 M^+ (33), 424 (7), 407 (42), 364 (49), 321 (16), 305 (4), 278 (6), 255 (7), 231 (6), 164 (18), 151 (100), 103 (5), 90 (4), 77 (6), 60 (27), 43 (25)
IIh	523 M^+ (2), 463 (37), 421 (38), 379 (100), 362 (5), 337 (85), 336 (65), 320 (17), 308 (7), 293 (24), 277 (9), 266 (10), 251 (11), 244 (9), 227 (7), 202 (23), 159 (13), 136 (25), 119 (11), 109 (10), 103 (8), 93 (15), 90 (12), 77 (12), 60 (39), 43 (78)
IIi	397 M^+ (32), 354 (13), 348 (5), 338 (7), 320 (5), 316 (6), 311 (5), 295 (7), 294 (13), 274 (93), 261 (5), 255 (7), 251 (13), 239 (6), 235 (5), 228 (7), 223 (9), 211 (14), 195 (10), 185 (28), 169 (10), 158 (7), 132 (10), 131 (9), 130 (10), 129 (10), 119 (11), 103 (12), 102 (10), 94 (17), 90 (12), 81 (10), 77 (11), 65 (20), 60 (20), 45 (28), 43 (100)
IIj	446 M^+ (4), 428 (7), 387 (22), 386 (85), 344 (43), 343 (87), 326 (13), 316 (6), 300 (22), 284 (6), 272 (8), 258 (26), 234 (7), 219 (5), 210 (11), 194 (10), 185 (6), 167 (22), 159 (9), 144 (43), 134 (65), 131 (52), 118 (54), 108 (17), 103 (15), 90 (28), 78 (33), 65 (22), 50 (32), 43 (100)
IIk	433 M^+ (12), 399 (5), 391 (19), 390 (33), 373 (3), 363 (4), 356 (7), 343 (12), 342 (70), 330 (15), 313 (12), 309 (7), 287 (20), 274 (18), 259 (16), 247 (15), 245 (15), 221 (25), 181 (6), 169 (13), 144 (12), 158 (10), 156 (9), 144 (10), 143 (9), 129 (25), 115 (38), 103 (20), 91 (28), 77 (27), 65 (19), 51 (16), 43 (100)
IIl	451 M^+ (37), 408 (14), 392 (8), 376 (5), 374 (6), 364 (4), 348 (12), 331 (10), 316 (6), 305 (16), 293 (5), 274 (57), 265 (12), 263 (10), 239 (21), 219 (4), 148 (28), 135 (100), 119 (8), 102 (7)

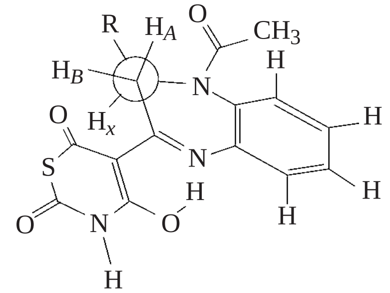
(three doublets of doublets which were not always resolved well): δ_X 4.80–5.23 ppm, $J_{AX} \approx 11.5$, $J_{BX} \approx$ 2–3.5 Hz; δ_B 3.55–4.17 ppm, $J_{AB} \approx$ 12.2–13.7, $J_{BX} \approx$ 2–3.5 Hz (in some cases, the J_{BX} value is almost equal to zero, for the dihderal angle $H_XC^2C^3H_B$ approaches 90°; therefore, the doublet of doublets degenerates into a pseudodoublet); δ_A 2.99–3.23 ppm, $J_{AB} \approx$ 12.2–13.7, $J_{AX} \approx$ 9.2– 11.5 Hz (insofar as J_{AB} and J_{AX} are very similar, a pseudotriplet is observed in most cases). Compounds **IIa**–**IIl** also displayed a singlet at δ 1.72–1.78 ppm from protons in the *N*-acetyl group, while NH signal typical of initial compounds **I** (δ 5.54–6.35 ppm) was absent.

The ^{13}C NMR spectra of acetylated benzodiazepines **IIa**–**IIl** in DMSO-d_6 (Table 4) contained signals from carbon atoms in the acetyl group (δ_C 169.0–169.7, 22.4–22.9 ppm), 1,5-benzodiazepine ring (C^2, δ_C 60.6– 67.3 ppm; C^3, δ_C 33.6–39.5 ppm), *o*-phenylenediamine fragment, substituent on C^2, and 1,3-thiazine ring. The signal intensity of carbon nuclei in the thiazine fragment of compounds **IIa**–**IIl** was so low that it was necessary to considerably increase the scan number to detect them. It seems quite surprising that acylation of distant N^1 atom dramatically affects the relaxation period of carbon nuclei in the thiazine ring. Nevertheless, this pattern was typical of all compounds **IIa**–**IIl**.

Acylated benzodiazepines **IIa**–**IIl** showed in the IR spectra (KBr, Table 5) absorption bands corresponding to stretching vibrations of the NH and OH groups involved in hydrogen bonding (3120–3380 cm^{-1}) and C=O and C=N groups (1600–1700 cm^{-1}).

All benzodiazepines **IIa**–**IIl** displayed light blue fluorescence upon irradiation with UV light. The UV spectra recorded from solutions in 96.5% ethanol contain two strong absorption bands with their maxima at λ 207–219 and 336–339 nm (initial benzo-

Table 3. ^{1}H NMR spectra of 5-(1-acetyl-2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-4-hydroxy-2*H*-1,3-thiazine-2,6-diones **IIa–IIl**



Comp. no.	δ, ppm (*J*, Hz)						
	OH, br.s	NH, br.s	H_X, d.d	H_B, d.d	H_A, t^a	Ac, s	Ar, R
IIa	13.58	12.03	6.23 (J_{AX} 13.4, J_{BX} 3.3)	4.05 (J_{AB} 12.9, J_{BX} 3.3)	2.65 (*J* 13.1)	1.74	7.52–7.60 m (3H), 7.49 d.t (1H, *J* 1.3, 7.5), 7.26–7.40 m (5H)
IIb	13.98	11.85	6.21 (J_{AX} 13.3, J_{BX} 3.5)	4.13 (J_{AB} 13.0, J_{BX} 3.5)	2.68 (*J* 13.1)	1.75	7.53 d.t (1H, *J* 1.2, 7.5), 7.48 d.d (1H, *J* 1.2, 8.1), 7.44 d.t (1H, *J* 1.2, 7.5), 7.40 d.d (1H, *J* 1.2, 8.1), 7.20 d (2H, *J* 8.0), 7.10 d (2H, *J* 8.0), 2.32 s (3H)
IIc	13.61	12.05	6.18 (J_{AX} 13.3, J_{BX} 3.4)	3.97 (J_{AB} 12.6, J_{BX} 3.4)	2.65 (*J* 13.1)	1.72	7.58 d.t (1H, *J* 1.2, 7.5), 7.54 d.d (1H, *J* 1.2, 8.1), 7.48 d.t (1H, *J* 1.2, 7.5), 7.45 d.d (1H, *J* 1.2, 8.1), 7.23 d (2H, *J* 8.0), 6.90 d (2H, *J* 8.0), 3.73 s (3H)
IId	13.91	11.79	6.19 (J_{AX} 13.3, J_{BX} 3.4)	4.09 (J_{AB} 12.6, J_{BX} 3.4)	2.62 (*J* 13.1)	1.72	7.53 d.t (1H, *J* 1.2, 7.5), 7.48 d.d (1H, *J* 1.2, 8.1), 7.43 d.t (1H, *J* 1.2, 7.5), 7.32 d.d (1H, *J* 1.2, 8.1), 7.10 d (2H, *J* 8.7), 6.61 d (2H, *J* 8.7), 2.92 s (6H)
IIe	13.96	11.86	6.02 (J_{AX} 13.2, J_{BX} 3.3)	4.15 (J_{AB} 12.5, J_{BX} 3.3)	2.63 (*J* 13.1)	1.76	7.42–7.57 m (4H), 7.35 d (2H, *J* 8.5), 7.31 d (2H, *J* 8.5)
IIf	13.93	11.83	6.23 (J_{AX} 13.2, J_{BX} 3.3)	4.16 (J_{AB} 12.8, J_{BX} 3.3)	2.66 (*J* 13.1)	1.78	7.54 d.t (1H, *J* 1.2, 7.5), 7.46 d.d (1H, *J* 1.2, 8.1), 7.42 d.t (1H, *J* 1.2, 7.5), 7.39 d.d (1H, *J* 1.2, 8.1), 7.36 d (2H, *J* 8.6), 7.03 d (2H, *J* 8.6), 2.27 s (3H)
IIg	13.58	12.02	6.19 (J_{AX} 13.2, J_{BX} 3.4)	3.98 (J_{AB} 12.7, J_{BX} 3.4)	2.67 (*J* 13.2)	1.73	7.45–7.61 m (3H), 6.90 d (2H, *J* 8.1), 6.83 d (2H, *J* 8.1), 3.72 s (3H), 3.70 s (3H)
IIh	13.58	12.04	6.21 (J_{AX} 13.1, J_{BX} 2.7)	4.06 (J_{AB} 12.7, J_{BX} 2.7)	2.67 (*J* 13.2)	1.76	7.47–7.60 m (4H), 7.20–7.28 m (3H), 2.28 s (3H), 2.27 s (3H)
IIi	13.91	11.85	6.32 (J_{AX} 13.6, J_{BX} 3.2)	4.15 (J_{AB} 12.7, J_{BX} 2.7)	2.66 (*J* 13.0)	1.74	7.53 d.t (1H, *J* 1.2, 7.5), 7.47 d.d (1H, *J* 1.2, 8.1), 7.39– 7.44 m (2H), 7.30 d.d (1H, *J* 1.2, 8.1), 6.32–6.35 m (2H)
IIj	13.64	12.03	6.69 (J_{AX} 13.0, J_{BX} 3.8)	4.20 (J_{AB} 12.5, J_{BX} 3.8)	2.72 (*J* 12.8)	1.70	11.01 d (1H, *J* 2.2), 7.79 d (1H, *J* 7.9), 7.53–7.59 m (2H), 7.40–7.45 m (1H), 7.36 d (1H, *J* 8.1), 7.31 d (1H, *J* 7.9), 7.20 d (1H, *J* 2.2), 7.10 d.t (1H, *J* 1.1, 7.5), 7.01 d.t (1H, *J* 1.1, 7.5)

Table 3. (Contd.)

Comp. no.	δ, ppm (*J*, Hz)						
	OH, br.s	NH, br.s	H_X, d.d	H_B, d.d	H_A, t[a]	Ac, s	Ar, R
IIk	13.91	11.82	5.89 m (1H)	4.04 (J_{AB} 12.2, J_{BX} 4.0)	2.37 (*J* 12.6)	1.76	7.50–7.55 m (2H), 7.42 m (2H), 7.38–7.41 m (2H), 7.27 t (2H, *J* 7.5), 7.19 d.t (1H, *J* 1.2, 7.5) 6.63 d (1H, *J* 15.9), 5.98 d.d (1H, *J* 6.1, 15.9)
IIl	13.93	11.85	6.13 (J_{AX} 13.2, J_{BX} 3.4)	4.08 (J_{AB} 12.7, J_{BX} 3.4)	2.61 (*J* 13.2)	1.74	7.40–7.57 m (4H), 6.72–6.84 m (3H), 5.96 s (2H)

[a] Pseudotriplet.

Table 4. ^{13}C NMR spectra of 5-(1-acetyl-2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-4-hydroxy-2*H*-1,3-thiazine-2,6-diones **IIa–IIl**, δ_C, ppm

Comp. no.	C^2	C^3	C^4	$C^{2'}$	$C^{4'}$	$C^{5'}$	$C^{6'}$	Ac	C^{5a}, C^6, C^7, C^8, C^9, C^{9a}R
IIa	63.6	36.5	181.6	170.8	167.5	97.8	162.8	169.4, 22.9	140.2, 134.1, 133.6, 131.1, 129.5, 128.7, 128.5, 127.6, 125.9, 125.4
IIb	63.6	36.2	181.6	170.7	167.6	97.9	162.7	169.3, 22.9	137.1, 136.8, 134.0, 133.6, 131.1, 129.5, 129.0, 128.7, 125.9, 125.4, 20.5
IIc	63.0	36.4	181.7	170.9	167.5	97.8	162.8	169.2, 22.4	158.6, 134.0, 133.6, 132.1, 131.1, 129.5, 128.7, 127.3, 125.4, 113.8, 55.0
IId	63.2	36.4	181.7	171.1	167.4	97.8	162.7	168.96, 22.9	149.8, 134.1, 133.6, 131.1, 129.4, 128.6, 127.5, 126.8, 125.3, 112.1, 39.99
IIe	62.96	36.2	181.9	170.2	167.7	97.9	162.7	169.5, 22.9	139.0, 133.8, 133.5, 132.2, 131.0, 129.6, 129.0, 128.5, 127.6, 125.5
IIf	63.2	36.5	181.8	170.7	167.5	97.8	162.8	169.1, 22.9	169.5, 149.8, 137.6, 133.9, 133.5, 131.1, 129.5, 128.8, 127.1, 125.5, 121.9, 20.7
IIg	63.3	36.5	181.8	170.9	167.5	97.8	162.8	169.3, 22.9	148.6, 148.3, 134.1, 133.6, 132.6, 131.2, 129.5, 128.7, 125.4, 118.3, 111.6, 109.9, 55.5, 55.3
IIh	62.8	36.3	181.9	170.5	167.7	97.8	162.7	169.7, 22.9	168.1, 168.0, 141.9, 141.3, 138.6, 133.8, 133.6, 131.1, 129.6, 128.8, 125.5, 124.0, 123.7, 121.2, 20.3, 20.2
IIi	57.2	34.4	181.7	170.1	167.6	98.1	162.7	169.0, 22.6	151.8, 142.7, 133.7, 133.5, 130.1, 129.7, 128.7, 125.3, 110.3, 106.8
IIj	57.5	36.2	181.8	171.3	167.5	98.6	162.7	168.7, 22.8	136.3, 134.1, 134.0, 131.0, 129.5, 128.6, 125.3, 125.2, 122.5, 121.3, 119.2, 118.7, 113.7, 111.4
IIk	61.9	35.4	181.7	171.1	167.6	98.0	162.8	169.0, 22.8	135.9, 133.8, 133.6, 131.1, 130.7, 129.5, 128.8, 128.5, 127.8, 126.6, 126.5, 125.2
IIl	63.3	36.4	181.6	170.8	167.4	97.8	162.7	169.3, 22.9	147.3, 146.6, 134.0, 133.6, 131.1, 131.2, 129.5, 128.7, 125.4, 119.5, 108.1, 106.5, 101.0

Table 5. UV and IR spectra of 5-(1-acetyl-2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-4-hydroxy-2*H*-1,3-thiazine-2,6-diones **IIa–IIl**

Comp. no.	UV spectrum (EtOH), λ_{max}, nm ($\varepsilon \times 10^{-4}$	IR spectrum (KBr), ν, cm^{-1}
IIa	209 (2.80), 338 (2.51)	436, 471, 491, 534, 542, 574, 595, 623, 638, 700, 716, 750, 771, 810, 831, 879, 897, 922, 955, 1050, 1078, 1091, 1112, 1158, 1209, 1223, 1279, 1315, 1329, 1351, 1365, 1381, 1412, 1446, 1458, 1494, 1556, 1580, 1602, 1619, 1659, 1667, 1680, 2369, 2839, 2899, 2930, 2975, 3050, 3171, 3423
IIb	208 (2.86), 221 (2.52), 340 (2.38)	437, 465, 487, 505, 531, 542, 554, 580, 592, 605, 621, 635, 642, 691, 722, 753, 770, 818, 837, 876, 897, 919, 952, 1036, 1059, 1090, 1113, 1157, 1185, 1212, 1225, 1278, 1297, 1318, 1350, 1365, 1379, 1411, 1446, 1459, 1494, 1515, 1556, 1579, 1601, 1618, 1657, 1666, 1680, 2839, 2921, 2974, 3037, 3165, 3365, 3435
IIc	204 (2.76), 226 (2.39), 340 (2.16)	433, 483, 543, 557, 580, 592, 606, 619, 639, 693, 712, 733, 754, 767, 811, 840, 876, 897, 918, 949, 957, 1025, 1049, 1089, 1113, 1153, 1159, 1181, 1208, 1223, 1224, 1250, 1277, 1319, 1348, 1366, 1382, 1411, 1459, 1494, 1515, 1556, 1579, 1602, 1611, 1655, 1666, 1680, 2365, 2833, 2930, 2976, 3050, 3167, 3446
IId	206 (2.74), 260 (1.68), 339 (1.82)	421, 450, 503, 534, 546, 561, 571, 588, 598, 650, 660, 678, 687, 730, 749, 768, 815, 832, 855, 887, 940, 957, 976, 1003, 1027, 1046, 1071, 1087, 1120, 1170, 1235, 1266, 1278, 1317, 1352, 1366, 1374, 1414, 1433, 1447, 1455
IIe	205 (2.79), 223 (2.75), 341 (2.34)	409, 425, 444, 479, 506, 527, 538, 556, 570, 582, 596, 649, 685, 723, 749, 764, 839, 859, 896, 944, 977, 1014, 1069, 1090, 1231, 1278, 1315, 1375, 1415, 1452, 1494, 1593, 1660, 1668, 1727, 2807, 2848, 2899, 3014, 3079, 3131, 3302, 3447
IIf	206 (2.83), 338 (2.20)	417, 432, 448, 502, 530, 559, 570, 586, 647, 657, 688, 696, 725, 751, 764, 776, 799, 824, 842, 866, 878, 907, 940, 974, 1017, 1035, 1047, 1069, 1086, 1102, 1168, 1190, 1220, 1276, 1298, 1314, 1347, 1370, 1348, 1444, 1455, 1494, 1507, 1595, 1663, 1667, 1678, 1717, 1770, 2367, 2854, 2922, 3064, 3082, 3207, 3424
IIg	208 (2.81), 275 (2.04)	416, 433, 469, 505, 535, 573, 612, 633, 646, 654, 685, 702, 733, 753, 760, 774, 795, 823, 837, 856, 898, 980, 1016, 1074, 1092, 1111, 1130, 1179, 1232, 1256, 1270, 1289, 1311, 1339, 1377, 1388, 1414, 1453, 1462, 1496, 1508, 1595, 1627, 1666, 1716, 2822, 2847, 2932, 2977, 2998, 3028, 3092, 3150, 3188, 3312, 3426
IIh	206 (2.81), 337 (2.01)	421, 436, 540, 551, 573, 588, 650, 696, 754, 765, 773, 802, 841, 895, 902, 941, 1010, 1113, 1173, 1183, 1205, 1263, 1283, 1318, 1342, 1374, 1415, 1450, 1497, 1507, 1596, 1656, 1699, 1717, 1772, 2382, 2849, 2942, 3054, 3166, 3434, 3504
IIi	214 (2.86), 339 (2.61)	417, 431, 448, 513, 540, 571, 578, 600, 616, 646, 713, 742, 752, 762, 776, 808, 849, 885, 904, 920, 947, 976, 1015, 1147, 1240, 1271, 1309, 1339, 1374, 1437, 1447, 1456, 1493, 1504, 1597, 1625, 1670, 1714, 1954, 1990, 3097, 3205, 3423
IIj	219 (3.47), 336 (2.61)	408, 420, 443, 482, 513, 530, 542, 567, 583, 617, 635, 652, 667, 685, 700, 723, 752, 770, 824, 834, 873, 908, 946, 976, 1009, 1060, 1081, 1114, 1223, 1274, 1318, 1335, 1355, 1375, 1400, 1421, 1442, 1451, 1460, 1494, 1597, 1618, 1669, 1682, 1725, 2342, 2360, 2795, 2930, 2970, 3007, 3058, 3093, 3146, 3181, 3346
IIk	209 (2.88), 251 (2.04), 339 (1.94)	418, 466, 501, 533, 554, 572, 584, 652, 690, 742, 756, 771, 834, 897, 974, 987, 1036, 1080, 1108, 1118, 1159, 1234, 1275, 1320, 1384, 1413, 1449, 1497, 1595, 1648, 1699, 1717, 1949, 2848, 2920, 2972, 3023, 3051, 3080, 3128, 3163, 3433
IIl	206 (2.76), 236 (2.09), 336 (2.14)	434, 463, 489, 542, 554, 606, 647, 699, 727, 755, 772, 796, 808, 929, 942, 960, 1042, 1059, 1090, 1101, 1160, 1207, 1224, 1243, 1261, 1280, 1318, 1365, 1382, 1413, 1447, 1458, 1493, 1502, 1557, 1583, 1602, 1621, 1655, 1667, 2778, 2842, 2898, 3048, 3169, 3447

diazepines **I** are characterized by 3–4 absorption maxima at λ 208–218, 262–281, 312–316, and 359–382 nm, and their fluorescence is bright yellow to yellow–green).

On heating in boiling DMF for 0.5–1.5 h, acylated benzodiazepines **IIa**–**IIl** were converted into 6-substituted 7-acetyl-6,7-dihydropyrimido[1,6-*a*][1,5]-benzodiazepine-1,3-diones **IIIa**–**IIIl** (yield 75–93%)

Table 6. Yields, melting points, R_f values, and elemental analyses of 6-substituted 7-acetyl-6,7-dihydropyrimido[1,6-*a*][1,5]benzodiazepine-1,3-diones **IIIa–IIIl**

Comp. no.	Yield, %	mp, °C	R_f (acetone–hexane, 2:1)	Found, %			Formula	Calculated, %		
				C	H	N		C	H	N
IIIa	76	>300 (decomp.)	0.61	69.22	4.92	12.11	$C_{20}H_{17}N_3O_3$	69.15	4.93	12.10
IIIb	79	294–296	0.55	69.89	5.31	11.59	$C_{21}H_{19}N_3O_3$	69.79	5.30	11.63
IIIc	83	272–273	0.52	66.76	5.06	11.15	$C_{21}H_{19}N_3O_4$	66.83	5.07	11.13
IIId	86	266–267	0.57	67.57	5.68	14.37	$C_{22}H_{22}N_4O_3$	67.68	5.68	14.35
IIIe	71	293–295	0.50	62.97	4.21	11.03	$C_{20}H_{16}N_3O_3Cl$	62.91	4.22	11.01
IIIf	74	249–250	0.48	65.12	4.71	10.39	$C_{22}H_{19}N_3O_5$	65.18	4.72	10.37
IIIg	76	296–298	0.45	64.81	5.19	10.29	$C_{22}H_{21}N_3O_5$	64.86	5.20	10.31
IIIh	73	224–225	0.43	62.32	4.57	9.05	$C_{24}H_{21}N_3O_7$	62.20	4.57	9.07
IIIi	68	>300 (decomp.)	0.47	64.03	4.49	12.43	$C_{18}H_{15}N_3O_4$	64.09	4.48	12.46
IIIj	82	>300 (decomp.)	0.31	68.35	4.71	14.54	$C_{22}H_{18}N_4O_3$	68.38	4.70	14.50
IIIk	67	277–279	0.29	70.68	5.14	11.27	$C_{22}H_{19}N_3O_3$	70.76	5.13	11.25
IIIl	78	286–288	0.47	64.51	4.39	10.75	$C_{21}H_{17}N_3O_5$	64.45	4.38	10.74

that are derivatives of previously unknown pyrimido[1,6-*a*][1,5]benzodiazepine fused heterocyclic system (Scheme 1). The structures of the products were confirmed by their elemental analyses (Table 6) and ^{1}H and ^{13}C NMR, UV, IR, and mass spectra.

In the mass spectra of compounds **IIIa**–**IIIl** (Table 7) we observed the molecular ion peak and peaks from fragment ions $[M - 43]^+$ (this peak is often the base one; it corresponds to loss of acetyl fragment) and $[M - R]^+$ (elimination of the aryl substituent as a result of cleavage of the C^6–C_{arom} bond).

The ^{1}H NMR spectra of **IIIa**–**IIIl** in DMSO-d_6 (Table 8) contained a slightly broadened singlet from the N^{2}H proton (δ 11.41–11.57 ppm; δ 8.51–8.92 ppm in $CDCl_3$) in the pyrimidine fragment; in some cases, this signal is split into a doublet ($J \approx 2.0$ Hz) due to long-range *W*-coupling with 4-H. The 4-H proton resonated as a doublet at δ 5.78–5.96 ppm with a small coupling constant *J* of about 1.8–2.0 Hz (in some cases, this doublet degenerates to a singlet). Aromatic proton signals appeared as overlapped multiplets at δ 6.23–7.68 ppm, and protons in the C^5H_2–C^6H gave rise each to a doublet of doublets belonging to an

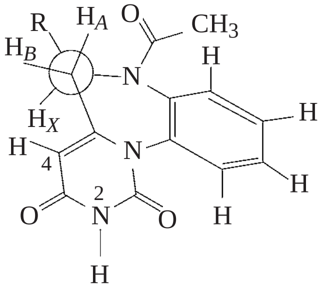
Table 7. Mass spectra of 7-acetyl-6-R-6,7-dihydropyrimido[1,6-*a*][1,5]benzodiazepine-1,3-diones **IIIa–IIIl**

Comp. no.	*m/z* (I_{rel}, %)
IIIa	347 M^+ (62), 305 (42), 304 (100), 288 (5), 261 (20), 245 (5), 233 (10), 228 (3), 221 (3), 201 (12), 195 (7), 185 (4), 180 (3), 159 (12), 58 (10), 157 (11), 134 (6), 133 (7), 132 (5), 119 (5), 103 (7), 90 (6), 78 (16), 73 (22), 43 (28)
IIIb	361 M^+ (56), 319 (47), 318 (100), 304 (13), 302 (9), 275 (29), 259 (7), 247 (8), 233 (7), 209 (16), 201 (15), 194 (5), 185 (4), 159 (16), 158 (14), 157 (17), 141 (4), 130 (17), 117 (18), 103 (16), 91 (20), 77 (20), 73 (11), 65 (10), 43 (53)
IIIc	377 M^+ (58), 335 (50), 334 (100), 320 (6), 319 (4), 318 (8), 304 (5), 291 (30), 277 (6), 276 (4), 275 (8), 263 (7), 251 (5), 249 (7), 225 (10), 219 (8), 210 (7), 201 (14), 185 (8), 159 (12), 158 (13), 157 (15), 134 (18), 130 (13), 121 (14), 119 (12), 115 (10), 103 (15), 90 (19), 77 (21), 65 (14), 51 (8), 43 (66)
IIId	390 M^+ (100), 375 (4), 347 (76), 333 (6), 304 (20), 290 (5), 276 (4), 262 (5), 241 (10), 240 (9), 214 (12), 198 (8), 185 (7), 171 (4), 170 (5), 157 (6), 148 (28), 147 (30), 146 (28), 134 (40), 120 (8), 103 (7), 90 (12), 77 (14), 44 (34), 43 (10)

Table 7. (Contd.)

Comp. no.	*m/z* (I_{rel}, %)
IIIe	383 M^+ (17), 382 M^+ (10), 381 M^+ (43), 338 (100), 324 (8), 323 (6), 322 (7), 297 (8), 295 (24), 281 (7), 280 (5), 279 (6), 267 (9), 255 (5), 229 (12), 214 (5), 201 (19), 185 (4), 159 (19), 158 (17), 157 (18), 130 (26), 103 (19), 90 (18), 77 (17), 67 (15), 65 (13), 63 (13), 51 (15), 43 (97)
IIIf	405 M^+ (50), 363 (49), 362 (39), 321 (48), 320 (100), 304 (17), 277 (33), 265 (9), 249 (13), 235 (8), 211 (11), 200 (9), 201 (14), 171 (4), 159 (14), 158 (16), 157 (16), 130 (17), 119 (9), 115 (5), 103 (7), 90 (6), 77 (8), 73 (41), 65 (7), 42 (54), 43 (85)
IIIg	407 M^+ (80), 363 (46), 364 (100), 350 (8), 334 (6), 321 (17), 305 (7), 201 (8), 165 (9), 164 (7), 163 (7), 151 (6), 130 (5), 119 (4), 103 (5), 90 (5), 77 (6), 43 (22)
IIIh	463 M^+ (23), 421 (34), 379 (100), 337 (88), 336 (68), 320 (14), 293 (20), 277 (5), 265 (6), 244 (7), 227 (8), 203 (14), 130 (11), 119 (8), 103 (6), 93 (5), 77 (6), 67 (8), 51 (6), 43 (95)
IIIi	337 M^+ (56), 295 (37), 294 (100), 280 (9), 278 (13), 237 (8), 136 (6), 235 (8), 224 (13), 223 (15), 219 (5), 201 (9), 195 (12), 185 (10), 170 (9), 158 (15), 157 (17), 130 (13), 119 (4), 103 (12), 90 (19), 77 (16), 73 (12), 65 (21), 43 (74)
IIIj	386 M^+ (100), 344 (50), 343 (82), 329 (10), 300 (24), 286 (6), 272 (8), 258 (7), 234 (6), 219 (6), 210 (7), 201 (6), 194 (8), 180 (4), 167 (6), 159 (6), 144 (20), 143 (25), 142 (18), 130 (26), 115 (20), 103 (8), 83 (16), 77 (14), 43 (40)
IIIk	373 M^+ (38), 331 (65), 330 (100), 316 (8), 287 (25), 282 (80), 259 (9), 254 (8), 245 (5), 227 (4), 221 (3), 206 (10), 184 (4), 169 (5), 157 (9), 144 (6), 130 (25), 115 (23), 103 (8), 92 (16), 77 (15), 65 (6), 51 (5), 43 (50)
IIIl	391 M^+ (24), 335 (50), 334 (100), 320 (6), 319 (4), 318 (8), 304 (5), 291 (30), 277 (6), 276 (4), 275 (8), 263 (7), 251 (5), 249 (7), 225 (10), 219 (8), 210 (7), 201 (14), 185 (8), 159 (12), 158 (13), 157 (15), 134 (18), 130 (13), 121 (14), 119 (12), 115 (10), 103 (15), 90 (19), 77 (21), 65 (14), 51 (8), 43 (66)

Table 8. ^{1}H NMR spectra of 7-acetyl-6-R-6,7-dihydropyrimido[1,6-*a*][1,5]benzodiazepine-1,3-diones **IIIa–IIIl** in DMSO-d_6



Comp. no.	Chemical shifts δ, ppm (*J*, Hz)						
	N^2H, s	C^4H	Ac, s	H_X, d.d	H_B, d.d	H_A, t[a]	Ar, R
IIIa	11.57	5.93 s	1.72	5.90 (*J* 4.9, 12.6)	3.20 (*J* 4.9, 13.9)	2.48 (*J* 13.2)	7.68 d.d (1H, *J* 1.2, 8.0), 7.57 d.t (1H, *J* 1.2, 7.6), 7.46 d.t (1H, *J* 1.2, 7.6), 7.24–7.36 m (6H)
IIIb	11.42	5.80 d (*J* 1.9)	1.74	5.89 (*J* 4.9, 12.7)	3.03 (*J* 4.9, 14.2)	2.51 (*J* 13.5)	7.63 d.d (1H, *J* 1.3, 8.1), 7.54 d.t (1H, *J* 1.3, 7.6), 7.42 d.t (1H, *J* 1.3, 7.6), 7.11 d.d (1H, *J* 1.3, 8.1), 7.08 s (4H), 2.32 s (3H)

Table 8. (Contd.)

Comp. no.	Chemical shifts δ, ppm (J, Hz)						
	N^{2}H, s	C^{4}H	Ac, s	H$_X$, d.d	H$_B$, d.d	H$_A$, t^a	Ar, R
IIIb^b	8.57	5.80 s	1.81	6.04 (J 4.8, 12.6)	2.82 (J 4.8, 14.2)	2.70 (J 13.4)	7.67 d.d (1H, J 1.2, 8.0), 7.57 d.t (1H, J 1.2, 7.6), 7.49 d.t (1H, J 1.2, 7.6), 7.11 d (2H, J 7.9), 7.07 d (2H, J 7.9), 7.01 d.d (1H, J 1.2, 8.0), 2.32 s (3H)
IIIc	11.42	5.80 d (J 2.0)	1.73	5.89 (J 4.9, 12.6)	3.10 (J 4.9, 13.9)	2.71 (J 13.3)	7.63 d.d (1H, J 1.3, 8.1), 7.54 d.t (1H, J 1.3, 7.6), 7.43 d.t (1H, J 1.3, 7.6), 7.11 m (3H), 6.80 d (2H, J 8.5), 3.76 s (3H)
IIIc^b	8.51 d (J 1.1)	5.80 d (J 2.0)	1.81	6.03 (J 5.0, 12.7)	2.81 (J 5.0, 14.0)	2.69 (J 13.4)	7.67 d.d (1H, J 1.3, 8.1), 7.57 d.t (1H, J 1.3, 7.6), 7.11 d (2H, J 8.7), 6.99 d.d (1H, J 1.3, 8.1), 6.83 d (2H, J 8.7), 3.79 s (3H)
IIId	11.41	5.78 d (J 2.0)	1.72	5.84 (J 5.0, 12.7)	2.98 (J 5.0, 14.1)	2.51 (J 13.3)	7.63 d.d (1H, J 1.3, 8.1), 7.54 d.t (1H, J 1.3, 7.6), 7.42 d.t (1H, J 1.3, 7.6), 7.08 d.d (1H, J 1.3, 8.1), 7.00 d (2H, J 8.7), 6.61 d (2H, J 8.7), 2.93 s (6H)
IIId^b	8.92	5.79 s	1.80	6.00 (J 5.1, 12.7)	2.78 (J 5.1, 14.1)	2.68 (J 13.4)	7.67 d.d (1H, J 1.3, 8.1), 7.55 d.t (1H, J 1.3, 7.6), 7.42 d.t (1H, J 1.3, 7.6), 7.04 d (2H, J 8.7), 7.01 d.d (1H, J 1.3, 8.1), 6.62 d (2H, J 8.7), 2.92 s (6H)
IIIe	11.44	5.80 d (J 2.0)	1.76	5.90 (J 4.9, 12.6)	3.10 (J 4.9, 13.9)	2.71 (J 13.3)	7.64 d.d (1H, J 1.3, 8.1), 7.55 d.t (1H, J 1.3, 7.6), 7.43 d.t (1H, J 1.3, 7.6), 7.29 d (2H, J 8.5), 7.25 d (2H, J 8.5), 7.17 d.d (1H, J 1.3, 8.1)
IIIe^b	8.71	5.81 d (J 1.9)	1.82	6.03 (J 4.9, 12.8)	2.83 (J 4.9, 14.1)	2.68 d.d (J 12.8, 14.1)	7.68 d.d (1H, J 1.3, 8.1), 7.58 d.t (1H, (1H, J 1.3, 7.6), J 1.3, 7.6), 7.45 d.t 7.29 d (2H, J 8.4), 7.14 d (2H, J 8.4), 6.99 d.d (1H, J 1.3, 8.1)
IIIf	11.44	5.82 d (J 1.8)	1.77	5.91 (J 4.8, 12.7)	3.09 (J 4.8, 13.9)	2.52 (J 13.1)	7.63 d.d (1H, J 1.3, 8.1), 7.55 d.t (1H, J 1.3, 7.6), 7.45 d.t (1H, J 1.3, 7.6), 7.27 d (2H, J 8.6), 7.23 d.d (1H, J 1.3, 8.1), 7.01 d (2H, J 8.6), 2.26 s (3H)
IIIg	11.58	5.91 s	1.70	5.83 (J 4.9, 12.6)	3.11 (J 4.9, 13.9)	2.51 d.d (J 12.6, 14.1)	7.68 d.d (1H, J 1.4, 7.9), 7.57 d.t (1H, J 1.4, 7.7), 7.48 d.t (1H, J 1.4, 7.7), 7.26 d.d (1H, J 1.4, 7.9), 6.88 d (1H, J 7.3), 6.73–6.77 m (2H), 3.72 s (3H), 3.68 s (3H)
IIIh	11.59	5.92 s	1.74	5.88 (J 4.8, 12.6)	3.25 (J 4.8, 13.9)	2.46 (J 13.3)	7.68 d.d (1H, J 1.4, 7.9), 7.57 d.t (1H, J 1.4, 7.7), 7.47 d.t (1H, J 1.4, 7.7), 7.34 d.d (1H, J 1.4, 7.9), 7.17–7.26 m (3H), 2.27 s, 2.26 s (6H)
IIIi	11.44	5.80 d (J 1.8)	1.76	6.01 (J 5.1, 2.5)	3.09 (J 5.1, 14.0)	2.65 (J 13.1)	7.61 d.d (1H, J 1.2, 8.0), 7.53 d.t (1H, J 1.2, 7.7), 7.43 d.t (1H, J 1.2, 7.7), 7.40 d (1H, J 1.8), 7.14 d.d (1H, J 1.2, 8.0), 6.31 d.d (1H, J 1.8, 3.2), 6.23 d (1H, J 3.2)

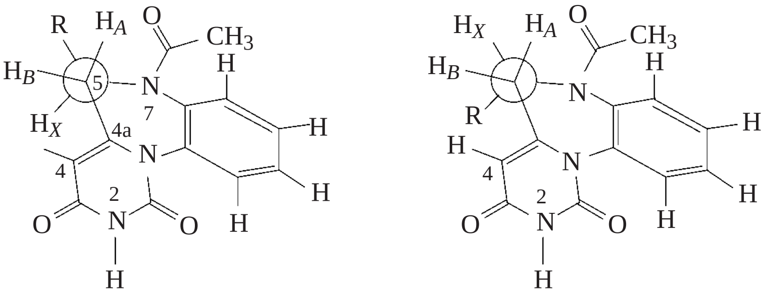
Table 8. (Contd.)

Comp. no.	Chemical shifts δ, ppm (J, Hz)						
	N^2H, s	C^4H	Ac, s	H_X, d.d	H_B, d.d	H_A, t[a]	Ar, R
IIIi[b]	8.58	5.80 d (J 2.1)	1.85	6.15 (J 5.1, 12.6)	2.90 (J 5.1, 14.1)	2.71 d.d (J 12.6, 14.1)	7.64 d.d (1H, J 1.4, 8.1), 7.55 d.t (1H, J 1.4, 7.6), 7.44 d.t (1H, J 1.3, 7.6), 7.30 d (1H, J 1.8), 7.06 d.d (1H, J 1.4, 8.1), 6.31 d.d (1H, J 1.8, 3.3), 6.23 d (1H, J 3.3)
IIIj	11.57 d (J 1.9)	5.96 d (J 1.9)	1.65	6.34 (J 5.2, 12.3)	3.17 (J 5.2, 13.8)	2.65 (J 13.0)	10.97 d (1H, J 1.5), 7.68 d.t (2H, J 1.2, 8.2), 7.55 d.t (1H, J 1.3, 7.7), 7.33–7.38 m (2H), 7.10 t (1H, J 7.5), 6.98–7.03 m (2H), 6.76 d.d (1H, J 1.2, 7.9)
IIIk[b]	8.68	5.79 d (J 1.9)	1.85	5.68 d.d.d (J 5.1, 7.1, 12.6)	2.77 (J 5.1, 14.1)	2.36 d.d (J 12.6, 14.1)	7.65 d.d (1H, J 1.3, 8.0), 7.57 d.t (1H, J 1.2, 7.8), 7.49 d.t (1H, J 1.2, 7.8), 7.26–7.35 m (6H), 6.65 d (1H, J 15.8), 5.98 d.d (1H, J 7.1, 15.8)
IIIl	11.56	5.82 d (J 1.9)	1.70	5.81 (J 4.8, 12.6)	3.10 (J 4.8, 13.9)	2.47 (J 13.4)	7.67 d.d (1H, J 1.4, 7.9), 7.57 d.t (1H, J 1.4, 7.7), 7.47 d.t (1H, J 1.4, 7.7), 7.25 d.d (1H, J 1.4, 7.9), 6.85 d (1H, J 8.1), 6.77 d (1H, J 1.5), 6.73 d.d (1H, J 1.5, 8.1), 5.99 s (2H)

[a] Pseudotriplet. [b] In $CDCl_3$.

ABX system: δ_X 5.84–6.34 ppm, $J_{AX} \approx$ 12.3–14.1, $J_{BX} \approx$ 4.8–5.2 Hz; δ_B 2.81–3.17 ppm, $J_{AB} \approx$ 13.8–14.2, $J_{BX} \approx$ 4.8–5.2 Hz; δ_A 2.65–2.71 ppm, $J_{AB} \approx$ 13.3–14.1, $J_{AX} \approx$ 12.6–12.8 Hz. The latter signal often looks like a pseudotriplet with a coupling constant $J \approx$ 13.0–13.4 Hz due to similar values of J_{AB} and J_{AX}. In addition, a three-proton singlet from the acetyl protons was observed at δ 1.65–1.85 ppm. The large difference in the coupling constants J_{AX} and J_{BX} ($J_{AX} >> J_{BX}$; the dihedral angle $H_XC^6C^5H_A$ approaches 180°, and the dihedral angle $H_XC^6C^5H_B$ is close to 70°) indicates that 6-substituted 7-acetyl-6,7-dihydropyrimido[1,6-*a*][1,5]benzodiazepine-1,3-diones **IIIa**–**IIIl** adopt conformation **A** rather than **B** (Scheme 2, a view along the C^5–C^6 bond). Otherwise, the dihedral angles $H_XC^6C^5H_A$ and $H_XC^6C^5H_B$ in conformer **B** would be similar, and the coupling constants J_{AX} and J_{BX} would also be similar, which contradicts the experimental data.

Scheme 2.



A **B**

In the IR spectra of crystalline compounds **IIIa**–**IIIl** (KBr, Table 9) we observed absorption bands in the regions 3120–3380 and 1600–1700 cm^{-1}, which belong to stretching vibrations of the N–H and C=O groups. The UV spectra of **IIIa**–**IIIl** in 96.5% ethanol are characterized (Table 9) by the presence of two absorption maxima at λ 209–218 and 271–275 nm (cf. λ 207–219 and 336–339 nm for initial compounds **II**).

Table 9. UV and IR spectra of 7-acetyl-6-R-6,7-dihydropyrimido[1,6-*a*][1,5]benzodiazepine-1,3-diones **IIIa**–**IIIl**

Comp. no.	UV spectrum (EtOH), λ_{max}, nm ($\varepsilon \times 10^{-4}$)	IR spectrum (KBr), ν, cm^{-1}
IIIa	208 (2.64), 272 (1.38)	415, 436, 505, 531, 550, 571, 594, 621, 646, 689, 710, 725, 747, 761, 773, 781, 840, 862, 879, 907, 946, 975, 1001, 1025, 1049, 1063, 1082, 1114, 1159, 1169, 1189, 1208, 1236, 1277, 1300, 1318, 1354, 1370, 1385, 1431, 1444, 1455, 1494, 1593, 1663, 1713, 2919, 2926, 3084, 3233, 3433
IIIb	214 (2.30), 221 (2.15), 272 (1.59)	414, 440, 500, 529, 540, 560, 571, 588, 606, 620, 648, 689, 723, 748, 762, 773, 818, 841, 864, 877, 909, 943, 974, 1016, 1047, 1068, 1085, 1113, 1165, 1187, 1236, 1275, 1317, 1369, 1384, 1444, 1494, 1593, 1667, 1713, 1950, 1988, 2925, 3053, 3086, 3208, 3428
IIIc	207 (2.65), 226 (1.68), 273 (1.37)	420, 459, 505, 532, 569, 595, 604, 621, 648, 666, 688, 717, 748, 763, 830, 859, 904, 943, 978, 1031, 1072, 1078, 1114, 1172, 1231, 1265, 1304, 1325, 1352, 1371, 1385, 1404, 1439, 1495, 1514, 1594, 1660, 1699, 1883, 1960, 2050, 2841, 3000, 3053, 3089, 3510
IIId	209 (2.81), 267 (2.08)	424, 458, 475, 499, 544, 579, 588, 603, 619, 638, 677, 692, 710, 754, 766, 814, 876, 914, 948, 1035, 1053, 1087, 1111, 1164, 1192, 1208, 1274, 1317, 1364, 1382, 1409, 1446, 1458, 1495, 1527, 1554, 1579, 1602, 1618, 1650, 1665, 1681, 2974, 3052, 3172, 3420
IIIe	209 (2.97), 223 (2.44), 273 (1.67)	424, 481, 527, 532, 586, 617, 637, 671, 703, 726, 754, 771, 808, 820, 836, 880, 896, 918, 956, 1014, 1051, 1089, 1109, 1158, 1183, 1195, 1207, 1222, 1278, 1317, 1351, 1365, 1380, 1410, 1446, 1458, 1493, 1454, 1582, 1658, 1664, 1677, 2977, 3044, 3171, 3422
IIIf	208 (2.83), 272 (1.38)	420, 435, 451, 492, 532, 544, 567, 588, 621, 634, 660, 700, 730, 755, 817, 824, 845, 910, 942, 957, 1007, 1016, 1035, 1061, 1092, 1117, 1164, 1197, 1240, 1279, 1320, 1337, 1354, 1369, 1382, 1415, 1449, 1466, 1497, 1507, 1547, 1587, 1624, 1639, 1672, 1769, 2819, 3019, 3115, 3436
IIIg	207 (2.62), 274 (1.06)	436, 449, 486, 542, 575, 602, 615, 648, 698, 752, 774, 787, 813, 862, 890, 917, 953, 966, 1026, 1065, 1092, 1113, 1140, 1160, 1205, 1219, 1253, 1280, 1318, 1367, 1412, 1444, 1458, 1495, 1519, 1558, 1581, 1588, 1603, 1655, 1666, 1682, 2839, 2933, 2958, 3001, 3041, 3164, 3444
IIIh	207 (2.75), 274 (1.19)	418, 436, 450, 472, 492, 540, 559, 588, 614, 638, 670, 701, 717, 754, 772, 813, 834, 846, 875, 899, 914, 950, 979, 1014, 1034, 1059, 1088, 1113, 1142, 1187, 1210, 1220, 1259, 1276, 1314, 1366, 1412, 1433, 1445, 1459, 1494, 1554, 1583, 1619, 1664, 1682, 1767, 1778, 2844, 3050, 3166, 3350, 3444
IIIi	219 (2.36), 273 (1.72)	417, 430, 447, 513, 540, 571, 600, 615, 646, 660, 679, 713, 722, 743, 752, 762, 775, 808, 849, 886, 905, 920, 947, 976, 1014, 1048, 1065, 1076, 1115, 1148, 1169, 1188, 1240, 1271, 1309, 1338, 1374, 1437, 1447, 1457, 1493, 1504, 1597, 1526, 1670, 1714, 1954, 1989, 2872, 3098, 3153, 3204, 3423
IIIj	218 (2.47), 271 (1.14)	422, 437, 476, 499, 540, 557, 578, 601, 620, 639, 689, 699, 712, 739, 762, 798, 810, 876, 898, 916, 950, 1011, 1022, 1035, 1048, 1073, 1084, 1109, 1132, 1160, 1203, 1214, 1276, 1287, 1317, 1362, 1412, 1458, 1495, 1553, 1581, 1601, 1622, 1651, 1668, 1680, 2840, 2929, 3048, 3174, 3366
IIIk	208 (2.58), 261 (1.89)	430, 485, 497, 519, 542, 585, 593, 616, 636, 660, 695, 753, 770, 808, 878, 887, 916, 952, 966, 989, 1032, 1058, 1076, 1110, 1157, 1203, 1214, 1275, 1315, 1365, 1380, 1410, 1446, 1457, 1494, 1555, 1578, 1601, 1620, 1666, 1681, 2837, 3024, 3048, 3082, 3166, 3365, 3453
IIIl	207 (2.65), 273 (1.37)	424, 442, 466, 485, 499, 537, 558, 573, 599, 623, 655, 695, 728, 756, 764, 774, 800, 816, 826, 843, 858, 879, 900, 930, 949, 974, 1038, 1073, 1090, 1123, 1159, 1172, 1235, 1250, 1263, 1287, 1321, 1379, 1390, 1409, 1440, 1497, 1596, 1650, 1706, 1716, 1730, 2846, 2887, 3056, 3129, 3162, 3442

Table 10. ^{13}C NMR spectra of 7-acetyl-6-R-6,7-dihydropyrimido[1,6-*a*][1,5]benzodiazepine-1,3-diones **IIIa**–**IIIl** in DMSO-d_6, δ_C, ppm

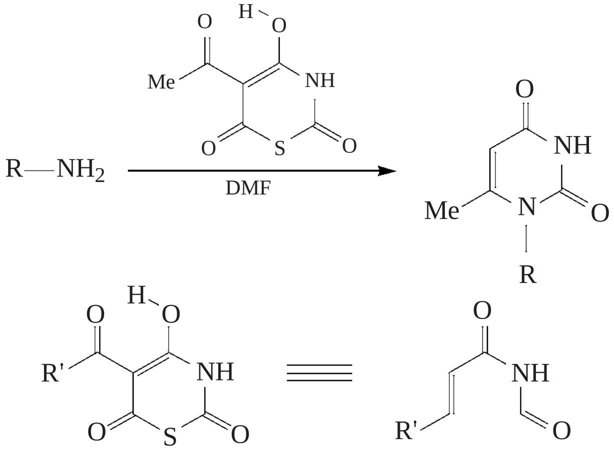
Comp. no.	C^1, C^3, C^{4a}	C^4	C^5	C^6	Ac	C^{7a}, C^8, C^9, C^{10}, C^{11}, C^{11a}, R
IIIa	162.55, 152.9, 150.2	101.04	35.2	59.1	169.2, 22.5	139.2, 133.5, 133.2, 130.5, 129.3, 129.1, 128.9, 128.3, 127.6, 126.7
IIIb	162.3, 152.5, 150.1	101.2	35.2	58.8	168.7, 22.5	136.8, 136.1, 133.5, 133.3, 130.5, 129.1, 128.9, 128.8, 128.7, 126.6, 20.6
IIIc	162.1, 158.7, 152.1	101.3	35.5	58.4	168.4, 22.4	150.0, 133.47, 133.44, 131.0, 130.4, 129.1, 128.59, 128.54, 127.86, 113.3, 54.7
IIId	162.1, 152.3, 150.0	101.2	35.5	58.5	168.1, 22.4	149.6, 133.61, 133.48, 130.4, 129.0, 128.49, 128.44, 127.42, 126.5, 111.7, 40.0
IIIe	162.1, 151.8, 150.0	101.5	35.2	58.4	168.7, 22.4	137.8, 133.37, 133.33, 132.7, 130.3, 129.2, 128.72, 128.67, 128.4, 128.04
IIIf	162.6, 152.8, 150.2	101.0	35.25	58.7	169.2, 22.5	169.0, 149.8, 136.7, 133.4, 133.2, 130.5, 129.4, 129.1, 128.98, 127.84, 121.65, 20.7
IIIg	162.6, 153.0, 150.3	100.96	35.4	58.9	168.97, 22.5	148.4, 148.3, 133.5, 133.2, 131.6, 130.7, 129.3, 129.0, 128.96, 118.95, 111.36, 110.7, 55.41, 55.33
IIIh	162.6, 152.7, 150.2	101.1	35.1	58.5	169.5, 22.5	168.12, 168.07, 141.75, 141.34, 137.8, 133.3, 133.2, 130.5, 129.4, 129.2, 129.1, 124.8, 123.5, 122.0, 20.48, 20.22
IIIi	162.0, 151.7, 151.2	101.7	33.9	52.7	168.3, 22.2	150.0, 141.8, 133.4, 133.3, 130.1, 129.0, 128.73, 128.69, 110.0, 107.1
IIIj	162.6, 153.2, 150.3	101.3	34.9	52.3	168.4, 22.3	136.3, 133.7, 133.3, 130.2, 129.1, 128.9, 125.7, 123.3, 121.3, 119.3, 118.7, 112.8, 111.4
IIIk	163.3, 153.5, 151.0	101.7	35.8	58.3	169.6, 23.2	136.7, 134.05, 133.97, 131.83, 131.26, 130.0, 129.96, 129.62, 129.26, 128.5, 127.2, 127.1
IIIl	162.5, 152.9, 150.2	100.7	35.2	58.8	169.0, 22.5	147.1, 146.6, 133.4, 133.2, 133.0, 130.5, 129.3, 129.04, 128.97, 128.93, 120.1, 107.9, 107.2

The ^{13}C NMR spectra of **IIIa**–**IIIl** in DMSO-d_6 (Table 10) contained the following signals, δ_C, ppm: 33.9–35.2 (C^5), 52.3–58.8 (C^6), 101.2–101.7 ppm (C^4), 168.1–168.7, and 22.2–22.5 (CH_3CO); also, signals from aromatic carbon atoms and C^{7a}–C^{11a} were present.

Heating of benzodiazepines **Ia**–**Il** in boiling dimethylformamide gave no expected 6-substituted 6,7-dihydropyrimido[1,6-*a*][1,5]benzodiazepine-1,3-diones. From the reaction mixtures we isolated 25–30% of 1-(2-aminophenyl)-6-[(*E*)-2-R-vinyl]uracils **IV**. Presumably, in this case the process also involves intermediate formation of pyrimido[1,6-*a*][1,5]benzodiazepine derivatives (Scheme 1), but the benzodiazepine ring therein undergoes cleavage to 6-vinyluracils **IV** which seem to be thermodynamically more stable.

Thus the results of the present study and our previous data on reactions of 5-acylthiazines with primary amines [2–4] and hydrazines [1] led to development of a novel, practically important, general, and selective method for the transformation of various types of primary amino groups into 1-substituted 6-alkyluracil derivatives using 5-acyl-4-hydroxy-2*H*-1,3-thiazine-2,6-diones as synthons in boiling dimethylformamide (Scheme 3). The proposed approach allowed us to synthesize in good yields tens previously unknown 1-substituted 6-alkyluracils, including 1-amino-6-methyluracil derivatives. Using 6-substituted 7-acetyl-6,7-dihydropyrimido[1,6-*a*]-[1,5]benzodiazepine-1,3-diones **IIIa**–**IIIl** as examples, we have demonstrated applicability of the proposed method for the synthesis of new fused heterocyclic systems. We can state that 5-acyl-4-hydroxy-2*H*-1,3-thiazine-2,6-diones represent a novel and convenient synthon of the structural fragment shown in Scheme 3.

Scheme 3.



R = Alk, Ar, AlkNH, ArNH, Alk$_2$N, Ar$_2$N, Alk(Ar)N, AlkCONH, ArCONH, R' = Me, Et, Pr.

EXPERIMENTAL

The mass spectra (electron impact, 70 eV) were recorded on an MKh-1321 mass spectrometer. The ^{1}H and ^{13}C NMR spectra were measured on a Bruker AM-500 instrument at 500 and 125 MHz, respectively, from solutions in DMSO-d_6 or CDCl$_3$. The IR spectra were recorded in KBr on an FSM 1201 spectrometer with Fourier transform. The UV spectra of solutions in 96.5% ethanol were obtained on an SF-2000 spectrophotometer (cell path length 1 cm). The progress of reactions and the purity of products were monitored by TLC using Sorbfil® plates. The melting points were determined in capillaries and were not corrected. The yields, melting points, and elemental analyses of compounds **IIa**–**IIl** and **IIIa**–**IIIl** are given in Tables 1 and 6.

5-Acetyl-4-hydroxy-3,6-dihydro-2*H*-1,3-thiazine-2,6-dione was synthesized according to the procedure described in [1].

5-[*N*-(2-Aminophenyl)ethanimidoyl]-4-hydroxy-2*H*-1,3-thiazine-2,6-dione [5]. A mixture of 1 g of finely powdered 5-acetyl-4-hydroxy-1,3-thiazine-2,6-dione and 580 mg of *o*-phenylenediamine in 25 ml of propan-2-ol was heated for 5–10 min under reflux. As a rule, the reactants initially dissolved, and almost colorless fine needles began to crystallize from the solution in 1–2 min after the boiling started. The mixture was cooled, and the precipitate was filtered off, washed with propan-2-ol, and dried in air. The product was analytically pure. Yield 1.45 g (98%), mp 197–198°C.

4-Hydroxy-5-(2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-2*H*-1,3-thiazine-2,6-diones Ia–**Il** *(general procedure)* [5]. Trifluoroacetic acid, 5–7 drops, was added to a mixture of 1 g of 5-[*N*-(2-aminophenyl)ethanimidoyl]-4-hydroxy-2*H*-1,3-thiazine-2,6-dione and 1.5–2 equiv of the corresponding aldehyde in 15 ml of propan-1-ol, and the mixture was heated for 1.5–2 h under reflux until the initial thiazine disappeared completely. The poorly soluble initial compound was gradually converted into a poorly soluble product which was a yellow finely crystalline and readily filterable powder. The mixture was cooled, and the precipitate was filtered off and washed with 2–3 portions of propan-1-ol. As a rule, compounds **Ia**–**Il** were analytically pure, and no additional purification was necessary.

1-Acetyl-5-(2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-4-hydroxy-2*H*-1,3-thiazine-2,6-diones IIa–**IIl** *(general procedure)* (Table 1). A mixture of 500 mg of 4-hydroxy-5-(2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-2*H*-1,3-thiazine-2,6-dione **Ia**–**Il** and 5 ml of acetic anhydride was heated for 0.5–1 h under reflux (TLC). Yellow benzodiazepines **Ia**–**Il** dissolved completely within 5–10 min after the mixture started to boil, and a colorless product began to crystallize from the solution almost immediately. The products were poorly soluble even in boiling acetic anhydride. The mixture was cooled, and excess acetic anhydride was distilled off on a rotary evaporator. The product was washed with ethanol and dried at 100°C. As a rule, compounds **IIa**–**IIl** were analytically pure, and no additional purification was necessary.

7-Acetyl-6-R-6,7-dihydropyrimido[1,6-*a*][1,5]-benzodiazepine-1,3-diones IIIa–**IIIl** *(general procedure)* (Table 6). A mixture of 500 mg of 1-acetyl-5-(2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-4-hydroxy-2*H*-1,3-thiazine-2,6-dione **IIa**–**IIl** and 10 ml of

DMF was heated under reflux until the reaction was complete (0.5–1.5 h, TLC). The process was accompanied by vigorous evolution of carbonyl sulfide which can be identified by characteristic odor (the DMF condensate was usually colored greenish–blue). The solvent was distilled off on a rotary evaporator, and the residue was recrystallized from ethanol–chloroform.

1-(2-Aminophenyl)-6-[(*E*)-2-(4-hydroxyphenyl)-vinyl]uracil (IVa). A mixture of 500 mg 4-hydroxy-5-[2-(4-hydroxyphenyl)-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl]-2*H*-1,3-thiazine-2,6-dione and 10 ml of DMF was heated under reflux until the reaction was complete (~2 h, TLC). The process was accompanied by evolution of carbonyl sulfide. The solvent was distilled off on a rotary evaporator, and the residue was recrystallized from ethanol. Yield 110 mg (26%), mp 187–188°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 11.25 s (1H), 7.23–7.30 m (2H), 7.04–7.11 m (3H), 6.98 d.d (1H, *J* = 1.3, 8.1), 6.82 d.t (1H, *J* = 1.3, 7.6), 6.71 d (2H, *J* = 8.6), 6.05 s (1H), 5.87 d (1H, *J* = 16.0), 4.92 br.s (3H). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 163.4, 158.9, 152.7, 151.0, 142.0, 136.7, 130.0, 129.9, 128.8, 126.1, 123.1, 119.2, 117.7, 115.7, 115.5, 97.0. Mass spectrum, *m/z* (I_{rel}, %): 321 $[M]^+$. Found, %: C 67.52; H 4.72; N 13.10; $C_{18}H_{15}N_3O_3$. Calculated, %: C 67.28; H 4.71; N 13.08.

1-(2-Aminophenyl)-6-[(*E*)-2-(4-methoxyphenyl)-vinyl]uracil (IVb). A mixture of 500 mg of 4-hydroxy-5-[2-(4-methoxyphenyl)-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl]-2*H*-1,3-thiazine-2,6-dione and 10 ml of DMF was heated under reflux until the reaction was complete (~2 h, TLC). The solvent was distilled off on a rotary evaporator, and the residue was recrystallized from ethanol. Yield 130 mg (30%), mp 163–164°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 11.05 s (1H), 7.20 d (1H, *J* = 16.0), 7.10–7.17 m (3H), 6.87 d.d (1H, *J* = 1.3, 8.1), 6.67–6.84 m (3H), 6.60 d.t (1H, *J* = 1.3, 7.6), 5.99 d (1H, *J* = 16.0), 5.95 s (1H), 5.11 br.s (2H), 3.75 s (3H). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 163.4, 160.2, 152.7, 151.0, 145.7, 136.0, 129.7, 128.5, 127.8, 120.7, 116.8, 115.9, 115.4, 114.5, 114.4, 97.1, 55.2. Mass spectrum, *m/z* (I_{rel}, %): 335 $[M]^+$. Found, %: C 68.14; H 5.12; N 12.51. $C_{19}H_{17}N_3O_3$. Calculated, %: C 68.05; H 5.11; N 12.53.

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