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Azines and Azoles: CXXIII.[1] Three-component Condensation of 5-Acetyl-4-hydroxy-3,6-dihydro-2*H*-1,3-thiazine-2,6-dione with *o*-Phenylenediamine and Carbonyl Compounds as a Convenient Synthesis of Substituted 1,5-Benzodiazepines

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Abstract — Readily accessible 5-acetyl-4-hydroxy-3,6-dihydro-2*H*-1,3-thiazine-2,6-dione reacted with an equimolar amount of *o*-phenylenediamine under mild conditions (propan-2-ol, 5 min, reflux) to give the corresponding Schiff base. Reactions of the latter with aldehydes and ketones in propan-1-ol in the presence of a catalytic amount of trifluoroacetic acid or in acetic acid led to the formation of 4-hydroxy-5-(2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-2*H*-1,3-thiazine-2,6-diones.
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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 (**I**) from malonic acid, potassium thiocyanate, and acetic anhydride in acetic acid [1–3]. We also found that thiazine **I** very readily reacts with various aliphatic and aromatic amines in ethanol or propan-2-ol at the acetyl carbonyl group without opening of the thiazine ring to afford only the corresponding Schiff bases [1, 2]. Reactions of 5-acetyl-4-hydroxy-3,6-dihydro-2*H*-1,3-thiazine-2,6-dione (**I**) with diamines were not studied. Therefore, it was not surprising that the reaction of thiazine **I** with an equimolar amount of *o*-phenylenediamine in boiling propan-2-ol (reaction time 5 min) gave 98% of compound **II**. It should be noted that heating of thiazine **I** with 1 equiv of *o*-phenylenediamine in boiling DMF was accompanied by extrusion of COS and formation of a 6-methyluracil derivative, 1-(2-aminophenyl)-6-methyluracil [1, 2] (Scheme 1).

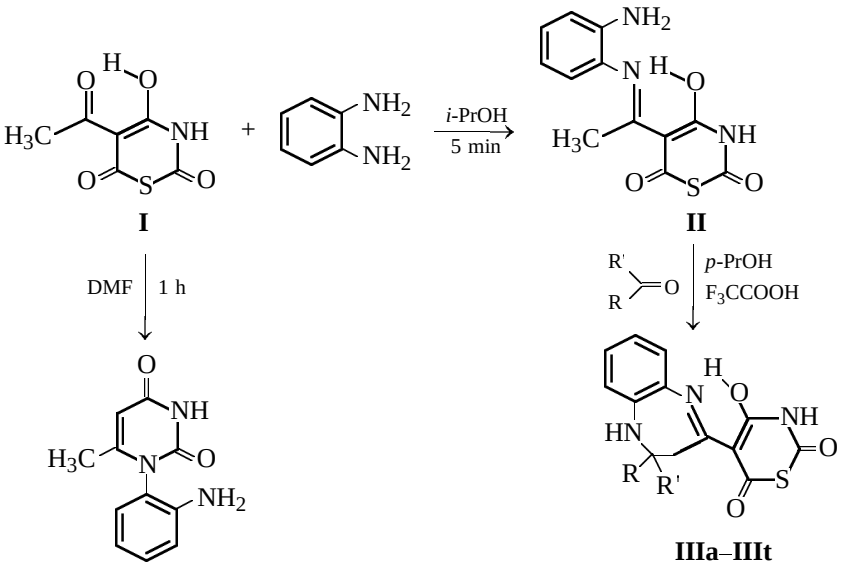
Our attention was attracted by the fact that a solution of **II** in acetone (prepared for TLC analysis) very quickly turned yellow (over a period of 2–3 days). According to the TLC data, a substance characterized by a higher R_f value than that of **II** (hexane–acetone, 2 : 1) accumulated in the acetone solution. This substance showed a bright yellow fluorescence under UV irradiation. We found that the product has the structure of 5-(2,2-dimethyl-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-4-hydroxy-2*H*-1,3-thiazine-2,6-dione (**IIIs**) rather than the expected Schiff base which could be formed via condensation at the free amino group of *o*-phenylenediamine. It turned out that the observed reaction is general and that it is catalyzed by acids.

1,5-Benzodiazepine derivatives [4–7] constitute an important class of biologically active substances w hich exhibit a broad spectrum of activity, depending on their structure [8]. Undoubtedly, preparation of previously unknown 1,5-benzodiazepine derivatives, especially of those containing pharmacophoric heterocyclic substituents, is of particular importance. In the present communication we describe the synthesis of 2,3-dihydro-1*H*-1,5-benzodiazepine derivatives having a 1,3-thiazine substituent in the 4-position.

2-Substituted 2,3-dihydro-1*H*-1,5-benzodiazepines **IIIa**–**IIIt** (Table 1) are formed by heating a mixture of compound **II** with a 1.5–2-fold excess of the corresponding aldehyde or ketone in boiling methanol, ethanol, propan-2-ol or propan-1-ol over a period of 1–3 h in the presence of a catalytic amount of trifluoroacetic acid. Propan-1-ol is the most preferred; it ensures the reaction to be complete in 1–1.5 h. A strong advantage of this procedure is very simple isolation of the product, which includes filtration of the cooled reaction mixture and washing of the precipitate with alcohol. According to the TLC data, ^{1}H and ^{13}C NMR, and mass spectra, and elemental analyses, the crude products were sufficiently pure. Under the given conditions, α,β-unsaturated aldehydes, such as croto-

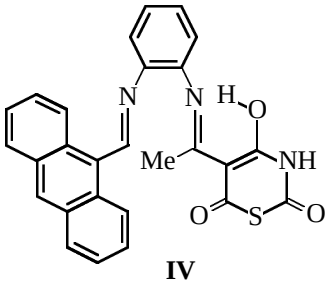
[1] For communication CXXII, see [1].

Scheme 1.



III, R = H; R' = Ph (**a**), 4-MeC_6H_4 (**b**), 4-HOC_6H_4 (**c**), 3,4-$(HO)_2C_6H_3$ (**d**), 4-$MeOC_6H_4$ (**e**), 3-MeO-4-$NO_2C_6H_3$ (**f**), β-piperonyl (**g**), 4-$Me_2NC_6H_4$ (**h**), 4-ClC_6H_4 (**i**), 2-ClC_6H_4 (**j**), 4-NCC_6H_4 (**k**), 4-$NO_2C_6H_4$ (**l**), 2-furyl (**m**), 3-indolyl (**n**), (*E*)-MeCH=CH (**o**), (*E*)-PhCH=CH (**p**), (*E*)-(2-furyl)–CH=CH (**q**), *i*-Pr (**r**); R = R' = Me (**s**); RR' = $(CH_2)_5$ (**t**).

naldehyde, cinnamaldehyde, and 3-(2-furyl)acrolein, and various heterocyclic aldehydes readily reacted with compound **II**. Among ketones, the reaction with cyclohexanone gave the best results; in the reaction of cyclopentanone a complex mixture consisting of five compounds was formed, and the composition of that mixture was not studied in the present work. From anthracene-9-carbaldehyde we obtained only Schiff base **IV** which did not undergo cyclization to the corresponding benzodiazepine even on prolonged heating (boiling propan-1-ol, 6 h).

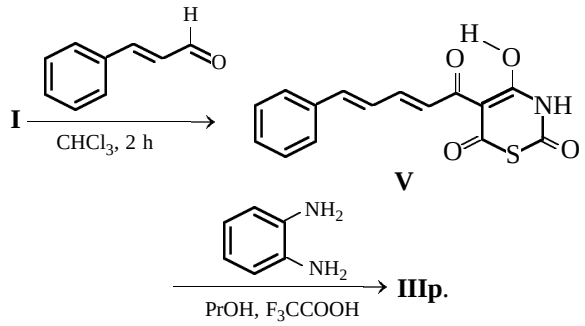


IV

The largest yields were obtained from aromatic aldehydes, especially from those having donor substituents in the aromatic ring. 4-Nitrobenzaldehyde failed to produce benzodiazepine derivative even on prolonged boiling in propan-1-ol (5 h). However, this problem was circumvented by heating a mixture of compound **II** with a small excess of 4-nitrobenzaldehyde in glacial acetic acid under reflux over a period of 1 h. Our attempts to effect the reaction with aliphatic aldehydes in boiling lower alcohols in the presence of trifluoroacetic acid were unsuccessful: the yields were as low as 2–5%. By heating isobutyraldehyde with compound **II** in boiling acetic acid over a period of 40 min we succeeded in isolating the corresponding benzodiazepine in 84% yield.

Benzodiazepine **IIIp** was also synthesized in 67% yield by an independent method (Scheme 2) from compound **V** and *o*-phenylenediamine in boiling propan-1-ol (reaction time 1.5 h). Compound **V** was prepared in 74% yield by heating a mixture of thiazine **I** and cinnamaldehyde in chloroform in the presence of catalytic amounts of pyridine and piperidine (it was isolated as lustrous leaflets resembling potassium dichromate in color); an analogous reaction with dehydroacetic acid was described in [9].

Scheme 2.



The structure of the isolated products was confirmed by the analytical data and ^1H and ^{13}C NMR,

Table 1. Yields, melting points, R_f values, and elemental analyses of 4-hydroxy-5-(2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-2*H*-1,3-thiazine-2,6-diones **IIIa**–**IIIt**, 4-hydroxy-5-{1-*N*-[2-(9-anthrylmethylideneamino)phenyl]ethanimidoyl}-2*H*-1,3-thiazine-2,6-dione (**IV**), and 4-hydroxy-5-[(2*E*,4*E*)-5-phenylpenta-2,4-dienoyl]-2*H*-1,3-thiazine-2,6-dione (**V**)

Comp. no.	Yield, %	mp, °C	R_f (acetone–hexane, 1 : 2)	Found, %			Formula	Calculated, %		
				C	H	N		C	H	N
II	98	197–198 (decomp.)	0.34	51.92	3.99	15.16	$C_{12}H_{11}N_3O_3S$	51.98	4.00	15.15
IIIa	70	239–240 (decomp.)	0.46	62.57	4.13	11.38	$C_{19}H_{15}N_3O_3S$	62.45	4.14	11.50
IIIb	75	236–237 (decomp.)	0.51	63.38	4.51	11.09	$C_{20}H_{17}N_3O_3S$	63.31	4.52	11.07
IIIc	68	245–246 (decomp.)	0.30	59.71	3.97	10.99	$C_{19}H_{15}N_3O_4S$	59.83	3.96	11.02
IIId	65	238–239 (decomp.)	0.14	57.38	3.81	10.56	$C_{19}H_{15}N_3O_5S$	57.42	3.80	10.57
IIIe	78	223–224	0.42	60.68	4.33	10.61	$C_{20}H_{17}N_3O_4S$	60.75	4.33	10.63
IIIf	92	237–238 (decomp.)	0.28	58.43	4.15	10.22	$C_{20}H_{17}N_3O_5S$	58.38	4.16	10.21
IIIg	76	219–221 (decomp.)	0.43	58.71	3.68	10.22	$C_{20}H_{15}N_3O_5S$	58.67	3.69	10.26
IIIh	81	247–248 (decomp.)	0.51	61.81	4.93	13.74	$C_{21}H_{20}N_4O_3S$	61.75	4.94	13.72
IIIi	60	244–245 (decomp.)	0.41	56.89	3.52	10.53	$C_{19}H_{14}ClN_3O_3S$	57.01	3.53	10.51
IIIj	54	205–206	0.41	56.91	3.53	10.50	$C_{19}H_{14}ClN_3O_3S$	57.01	3.53	10.51
IIIk	60	284–285 (decomp.)	0.37	61.59	3.60	14.33	$C_{20}H_{14}N_4O_3S$	61.53	3.61	14.35
IIIl	49	257–258 (decomp.)	0.43	55.65	3.43	13.67	$C_{19}H_{14}N_4O_5S$	55.60	3.44	13.65
IIIm	63	191–192	0.43	57.34	3.68	11.80	$C_{17}H_{13}N_3O_4S$	57.46	3.69	11.82
IIIn	65	255–256 (decomp.)	0.30	62.23	3.98	13.87	$C_{21}H_{16}N_4O_3S$	62.36	3.99	13.85
IIIo	57	192–193	0.41	58.22	4.58	12.78	$C_{16}H_{15}N_3O_3S$	58.34	4.59	12.76
IIIp	72	205–206	0.46	64.55	4.36	10.74	$C_{21}H_{17}N_3O_3S$	64.43	4.38	10.73
IIIq	71	220–222 (decomp.)	0.45	59.71	3.94	10.99	$C_{19}H_{15}N_3O_4S$	59.83	3.96	11.02
IIIr	84	210–211	0.61	58.06	5.15	12.66	$C_{16}H_{17}N_3O_3S$	57.99	5.17	12.68
IIIs	43	232–233 (decomp.)	0.46	56.65	4.76	13.26	$C_{15}H_{15}N_3O_3S$	56.77	4.76	13.24
IIIt	60	227–228 (decomp.)	0.73	61.50	5.68	11.33	$C_{19}H_{21}N_3O_3S$	61.44	5.70	11.31
IV	76	217–218	0.46	69.78	4.10	9.04	$C_{27}H_{19}N_3O_3S$	69.66	4.11	9.03
V	74	215–216 (decomp.)	0.53 [a]	59.64	3.69	4.64	$C_{15}H_{11}NO_4S$	59.79	3.68	4.65

[a] Eluent benzene–acetic acid, 10 : 1.

UV, IR, and mass spectra. The mass spectra of compounds **II**, **IIIa**–**IIIt**, **IV**, and **V** are given in Table 2. Almost all these showed the molecular ion peak in the mass spectrum. In addition, $[M - 60]^+$ ion peak was present due to expulsion of COS molecule from the molecular ion. The mass spectra also contained peaks from fragment ions arising from cleavage of the bonds between C^2 in the benzodiazepine ring and aryl substituent ($[M - R]^+$) and between C^4 in the benzodiazepine ring and C^5 in the thiazine ring ($[M - 144]^+$, *m/z* 144). In some cases, the fragmentation patterns were complicated by thermal decomposition of sam-

Table 2. Mass spectra of 4-hydroxy-5-(2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-2*H*-1,3-thiazine-2,6-diones **IIIa**–**IIIt**, 4-hydroxy-5-{1-*N*-[2-(9-anthrylmethylideneamino)phenyl]ethanimidoyl}-2*H*-1,3-thiazine-2,6-dione (**IV**), and 4-hydroxy-5-[(2*E*,4*E*)-5-phenylpenta-2,4-dienoyl]-2*H*-1,3-thiazine-2,6-dione (**V**)

Comp. no.	*m/z* (I_{rel}, %)
II	277 (M^+, 27%), 266 (85), 219 (12), 217 (7), 202 (15), 178 (4), 174 (4), 159 (15), 145 (7), 133 (100), 132 (80), 131 (40), 104 (7), 92 (24), 80 (12), 65 (29), 60 (20)
IIIa	366 (M^+ + 1, 23%), 365 (M^+, 100), 350 (4), 332 (15), 305 (10), 304 (15), 288 (8), 276 (9), 274 (12), 261 (21), 233 (21), 221 (36), 219 (36), 195 (51), 194 (59), 158 (15), 144 (19), 133 (17), 119 (34), 103 (25), 92 (21), 77 (29), 65 (27), 60 (23), 51(15), 39 (17)

Table 2. (Contd.)

Comp. no.	*m/z* (I_{rel}, %)
IIIb	380 (M^+ + 1, 23%), 379 (M^+, 100), 346 (19), 318 (10), 319 (12), 274 (19), 281 (19), 247 (19), 235 (38), 233 (28), 209 (71), 208 (72), 158 (19), 144 (19), 130 (19), 119 (47), 115 (19), 103 (33), 91 (33), 77 (28), 65 (43), 60 (12), 51 (11)
IIIc	381 (M^+, 10%), 321 (15), 320 (15), 277 (10), 235 (71), 210 (5), 159 (7), 134 (19), 118 (10), 115 (5), 103 (10), 93 (19), 77 (10), 65 (20), 60 (100), 51 (10)
IIId	397 (M^+, 18%), 363 (4), 337 (19), 336 (13), 319 (15), 301 (14), 293 (15), 278 (20), 277 (38), 253 (20), 252 (51), 251 (86), 233 (6), 227 (6), 217 (8), 205 (12), 168 (6), 159 (7), 158 (7), 144 (8), 136 (20), 134 (33), 132 (30), 119 (7), 110 (29), 103 (40), 92 (28), 77 (30), 64 (40), 60 (100)
IIId[a]	337 (M^+ – COS, 8%), 251 (20), 243 (6), 227 (6), 217 (8), 200 (8), 182 (3), 174 (6), 158 (16), 144 (4), 134 (52), 110 (30), 106 (24), 92 (10), 90 (8), 79 (24), 78 (24), 64 (28), 60 (8), 51 (10), 43 (100)
IIIe	395 (M^+, 71%), 362 (17), 335 (133), 334 (15), 291 (13), 271 (12), 263 (14), 251 (42), 239 (30), 225 (65), 224 (67), 201 (13), 185 (8), 159 (14), 144 (21), 134 (100), 121 (38), 119 (33), 103 (25), 91 (25), 77 (21), 65 (29), 60 (83), 51 (13)
IIIf	411 (M^+, 62%), 378 (10), 368 (4), 378 (10), 351 (38), 350 (34), 336 (4), 333 (7), 307 (19), 265 (45), 251 (14), 241 (38), 240 (40), 217 (24), 201 (14), 150 (57), 144 (15), 134 (17), 137 (12), 119 (22), 103 (20), 92 (10), 82 (10), 77 (17), 65 (22), 60 (100)
IIIg	410 (M^+ + 1, 28%), 409 (M^+, 100), 394 (5), 381 (4), 380 (5), 377 (7), 376 (17), 366 (9), 349 (19), 348 (19), 332 (6), 330 (9), 305 (20), 277 (24), 265 (40), 239 (68), 238 (82), 224 (8), 219 (11), 205 (10), 199 (8), 185 (9), 160 (12), 159 (14), 158 (13), 148 (74), 144 (30), 135 (34), 132 (20), 130 (18), 119 (16), 103 (26), 92 (18), 89 (18), 77 (24), 76 (16), 65 (30), 60 (32), 51 (16), 44 (15), 43 (56), 39 (24)
IIIh	409 (M^+ + 1, 28%), 408 (M^+, 100), 380 (8), 375 (10), 365 (5), 348 (35), 347 (25), 304 (20), 276 (18), 264 (58), 262 (30), 238 (10), 237 (9), 191 (10), 166 (11), 158 (10), 147 (98), 134 (70), 121 (15), 119 (15), 103 (15), 92 (8), 91 (9), 77 (18), 65 (13), 60 (30)
IIIi	401 (M^+, 41%), 400 (M^+, 25), 399 (M^+, 100), 366 (18), 339 (18), 338 (21), 327 (10), 310 (8), 295 (15), 274 (23), 267 (18), 257 (49), 255 (44), 228 (67), 227 (51), 219 (13), 220 (10), 200 (8), 185 (10), 159 (23), 144 (28), 132 (26), 119 (41), 103 (31), 93 (30), 77 (31), 65 (44), 60 (67), 51 (23)
IIIj	401 (M^+, 40%), 400 (M^+, 26), 399 (M^+, 100), 384 (4), 368 (5), 366 (16), 364 (24), 356 (4), 339 (22), 338 (14), 323 (4), 322 (4), 321 (4), 310 (6), 304 (8), 295 (12), 288 (10), 274 (24), 265 (18), 261 (22), 255 (42), 229 (50), 228 (74), 219 (50), 214 (10), 200 (8), 190 (8), 185 (12), 158 (24), 144 (18), 130 (24), 119 (70), 103 (36), 102 (34), 92 (36), 77 (34), 65 (46), 60 (64), 51 (22), 44 (14), 43 (12), 39 (30)
IIIk	390 (M^+, 29%), 374 (2), 372 (2), 357 (4), 347 (2), 330 (21), 329 (16), 313 (3), 289 (11), 274 (4), 258 (7), 246 (24), 245 (29), 244 (84), 220 (21), 219 (19), 214 (4), 202 (3), 185 (3), 171 (2), 159 (7), 158 (6), 144 (6), 140 (4), 134 (11), 131 (7), 122 (6), 119 (21), 116 (6), 108 (6), 103 (9), 102 (7), 93 (17), 92 (13), 77 (11), 65 (20), 60 (100), 52 (7), 51 (9), 45 (19), 44 (27), 43 (11)
IIIl	410 (M^+, 20%), 393 (11), 350 (9), 333 (2), 306 (4), 277 (8), 266 (7), 265 (15), 264 (37), 240 (6), 239 (8), 231 (4), 218 (28), 217 (10), 206 (4), 193 (4), 185 (2), 172 (2), 159 (6), 158 (7), 144 (8), 134 (12), 132 (11), 119 (10), 103 (8), 91 (10), 77 (9), 60 (100), 51 (9), 43 (25)
IIIm	355 (M^+, 61%), 338 (4), 327 (3), 322 (7), 312 (3), 395 (5), 294 (5), 274 (11), 267 (3), 261 (11), 250 (7), 223 (9), 211 (23), 185 (34), 158 (12), 156 (10), 144 (9), 130 (10), 119 (13), 103 (16), 94 (18), 81 (21), 77 (14), 65 (27), 60 (91), 45 (100)
IIIn	404 (M^+, 57%), 371 (7), 344 (25), 327 (8), 300 (16), 272 (15), 260 (35), 258 (25), 234 (30), 233 (23), 210 (8), 158 (12), 143 (100), 130 (40), 117 (20), 115 (22), 103 (12), 90 (12), 60 (35)
IIIo	329 (M^+, 100%), 314 (15), 301 (5), 296 (5), 288 (5), 286 (5), 274 (8), 269 (5), 261 (6), 254 (9), 237 (7), 230 (6), 225 (9), 215 (10), 211 (12), 197 (13), 185 (22), 183 (15), 169 (19), 159 (24), 158 (25), 144 (10), 132 (15), 119 (28), 108 (6), 103 (10), 92 (17), 91 (19), 77 (20), 65 (18), 60 (13), 51 (10), 45 (11), 41 (12), 39 (15)
IIIp	391 (M^+, 100%), 331 (10), 287 (10), 274 (15), 259 (13), 247 (25), 221 (15), 219 (15), 169 (37), 158 (15), 146 (10), 132 (20), 130 (25), 119 (25), 117 (20), 115 (25), 103 (15), 91 (20), 77 (23), 65 (25), 60 (50)
IIIq	381 (M^+, 100%), 353 (4), 348 (3), 338 (6), 321 (5), 282 (6), 277 (8), 274 (17), 249 (17), 237 (27), 219 (14), 211 (18), 196 (8), 183 (13), 177 (5), 169 (21), 158 (14), 144 (11), 132 (20), 120 (38), 119 (40), 107 (12), 103 (27), 102 (16), 92 (22), 91 (44), 81 (33), 77 (32), 65 (49), 51 (24), 44 (25), 43 (19), 41 (25), 39 (47)

Table 2. (Contd.)

Comp. no.	*m/z* (I_{rel}, %)
IIIr	331 (M^+, 36%), 288 (100), 271 (1), 270 (1), 260 (1), 254 (2), 245 (15), 228 (24), 211 (25), 201 (4), 185 (9), 170 (4), 157 (8), 156 (7), 155 (7), 143 (17), 119 (29), 102 (4), 92 (7), 77 (7), 65 (10), 60 (6), 51 (4), 45 (5), 43 (5), 41 (6), 39 (8)
IIIs	318 (M^+ + 1, 19%), 317 (M^+, 100), 302 (58), 274 (44), 261 (7), 259 (9), 242 (16), 225 (11), 199 (14), 185 (7), 173 (23), 157 (18), 144 (11), 133 (51), 103 (9), 92 (18), 77 (13), 65 (20), 41(20), 39 (16)
IIIt	358 (M^+ + 1, 22%), 357 (M^+, 100), 315 (13), 314 (48), 301 (8), 286 (13), 274 (6), 254 (13), 213 (35), 183 (11), 169 (31), 159 (11), 160 (15), 145 (27), 132 (27), 119 (11), 102 (11), 92 (13), 77 (15), 65 (17), 60 (4)
IV	405 (M^+ – COS, 3%), 361 (1), 334 (2), 320 (29), 319 (17), 262 (9), 216 (8), 202 (15), 178 (10), 160 (8), 133 (20), 132 (57), 131 (22), 92 (8), 85 (8), 65 (9), 60 (100), 43 (22)
V	301 (M^+, 22%), 283 (22), 258 (3), 255 (12), 241 (5), 240 (3), 224 (8), 223 (5), 214 (5), 112 (7), 198 (15), 197 (17), 184 (17), 173 (20), 170 (18), 157 (35), 145 (20), 141 (27), 130 (40), 129 (100), 128 (95), 127 (33), 118 (13), 115 (40), 102 (17), 91 (17), 77 (30), 69 (13), 60 (10), 51 (29), 44 (25), 43 (18), 39 (20)

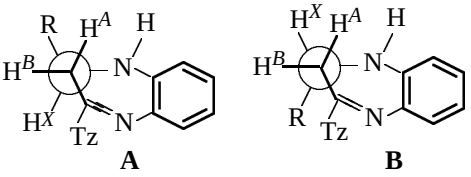
[a] Vaporizer temperature 250°C.

ples during vaporization with elimination of COS; this was typical of high-melting and low-volatile compounds **III** having an aryl substituent in the 2-position. For example, the mass spectrum of compound **IIId** recorded at a higher vaporizer temperature was the same as the mass spectrum of the product of thermal extrusion of COS from **IIId**.

In the ^{1}H NMR spectra of 1,5-benzodiazepines **IIIa**–**IIIt** in DMSO-d_6 (Table 3) we observed singlets from protons of the OH (δ 13.80–14.07 ppm) and NH groups (δ 11.65–11.85 ppm) in the thiazine ring, a relatively narrow singlet of the diazepine NH proton (δ 5.54–6.35 ppm), overlapping multiplets from protons in the benzene ring and aryl groups on C^2 in the benzodiazepine ring (δ 6.25–7.41 ppm). Also, an *ABX* pattern (not always clearly resolved) from the benzodiazepine 2-H and 3-H protons was present; it included a doublet of doublets from 2-H (*X*, δ 4.80–5.23 ppm; J_{AX} ~9.6–10.7, J_{BX} ~2.2?3.7 Hz); a doublet of doublets from 3-H (*B*, ~3.55–4.17 ppm; J_{AB} ~11.8–13.0, J_{BX} ~2.2–3.7 Hz; in some cases, the latter coupling constant is close to zero, obviously because the dihedral angle $HXC^2C^3H^B$ approaches 90°; therefore, the doublet of doublets is reduced to a pseudodoublet); and a doublet of doublets from 3-H^A (δ 2.99–3.23 ppm; J_{AB} ~11.8?13.0, J_{AX} ~9.6–10.7 Hz; due to similar values of J_{AB} and J_{AX}, a pseudotriplet is sometimes observed). The ^{1}H NMR spectra of **IIIa**–**IIIt** lack signal from acetyl protons, in contrast to initial compound **II** (δ 2.38 ppm, s, 3H).

The large difference between the coupling constants J_{AX} and J_{BX} ($J_{AX} >> J_{BX}$, the dihedral angle $HXC^2C^3H^A$approaches 180°, and the angle $HXC^2C^3H^B$ is close to 70°) suggests that 1,5-benzodiazepines **IIIa**–**IIIt** exist as conformer **A** rather than **B** (Scheme 3, a view along the C^3–C^2 bond). Otherwise (the dihedral angles $HXC^2C^3H^A$ and $HXC^2C^3H^B$ in conformer **B** are similar), the J_{AX} and J_{BX} values would approach each other, which is inconsistent with the experimental data (Table 3).

Scheme 3.

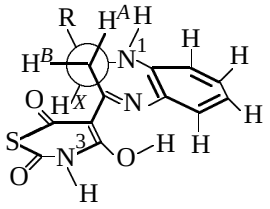


The ^{13}C NMR spectra of solutions of **IIIa**–**IIIt** in DMSO-d_6 (Table 4) contain signals typical of 1,5-benzodiazepine ring system, δ_C 60.6–67.3 (C^2) and 33.6–39.5 ppm (C^3) (no such signals were present in the spectra of initial compounds), as well as signals from carbon atoms in the 1,3-thiazine ring and substituent on C^2.

1,5-Benzodiazepines **IIIa**–**IIIt** showed in the IR spectra (KBr, Table 3) absorption bands in the regions corresponding to stretching and bending vibrations of NH and OH groups involved in hydrogen bonding (3120–3380 cm^{-1}) and stretching vibrations of C=O and C=N groups (1600–1700 cm^{-1}).

As noted above, all 1,5-benzodiazepines **IIIa**–**IIIt** show bright yellow to yellow-green fluorescence under UV irradiation. The UV spectra of solutions of **IIIa**–**IIIt** in 96.5% ethanol (Table 3) contain 4–5 absorption bands with their maxima at λ 208–218, 262–281, 312–316, and 359–382 nm; by contrast, initial

Table 3. UV, IR, and ^{1}H NMR spectra of 4-hydroxy-5-(2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-2*H*-1,3-thiazine-2,6-diones **IIIa**–**IIIt**, 4-hydroxy-5-{1-*N*-[2-(9-anthrylmethylideneamino)phenyl]ethanimidoyl}-2*H*-1,3-thiazine-2,6-dione (**IV**), and 4-hydroxy-5-[(2*E*,4*E*)-5-phenylpenta-2,4-dienoyl]-2*H*-1,3-thiazine-2,6-dione (**V**)



Comp. no.	UV spectrum, (EtOH), λ_{max}, nm ($\varepsilon \times 10^4$)	IR spectrum (KBr), ν, cm^{-1}	^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz)						
			OH	N^{3}H	N^{1}H	H^x	H^b	H^a	Ar, R
II	210 (2.70), 234 (2.18), 301 (2.29)	3470, 3395, 3320, 3225, 3120, 2946, 2790, 2360, 2340, 1665, 1620, 1544, 1350, 1248, 890, 755, 687, 540, 434	13.65 s (1H)	11.78 s (1H)	5.34 s (2H)	–	2.38 s (3H)		7.11 d.t (1H, *J* 1.2, 7.5), 7.03 d.d (1H, *J* 1.2, 8.1), 6.82 d.d (1H, *J* 1.2, 8.1), 6.62 d.t (1H, *J* 1.2, 7.5)
IIIa[a]	208 (1.91), 240 (1.02), 315 (0.87), 377 (0.68)	3365, 3030, 2985, 1677, 1607, 1588, 1567, 1490, 1455, 1408, 1369, 1340, 1300, 872, 758, 692, 638, 561, 446	13.98 s (1H)	11.58 s (1H)	6.13 s (1H)	5.26 d.d (1H, J_{ax} 10.7, J_{bx} 3.2)	3.94 pseudo-d (1H, J_{ab} 11.8)	3.16 d.d (1H, J_{ab} 11.8, J_{ax} 10.7)	7.38 d (2H, *J* 7.5), 7.32 t (2H, *J* 7.5), 7.25 t (1H, *J* 7.5), 7.12–7.18 m (3H), 6.90 d.t (1H, *J* 1.2, 7.5)
IIIb	210 (2.45), 240 (1.55), 276 (0.98), 315 (1.26)	3365, 2975, 2360, 1668, 1632, 1591, 1567, 1460, 1410, 1370, 1340, 1295, 1160, 862, 815, 740, 705, 630, 547, 470, 444	13.80 s (1H)	11.82 s (1H)	6.28 s (1H)	5.16 d.d (1H, J_{ax} 10.4, J_{bx} 2.3)	3.78 d.d (1H, J_{ab} 12.7, J_{bx} 2.3)	2.99 d.d (1H, J_{ab} 12.7, J_{ax} 10.4)	7.18–7.24 m (4H), 7.10–7.16 m (3H), 6.92 d.t (1H, *J* 1.2, 7.5), 2.27 s (3H)
IIIc	218 (2.72), 279 (1.62), 315 (1.95), 376 (1.51)	3330, 3020, 2880, 2360, 1685, 1615, 1560, 1515, 1480, 1453, 1340, 1222, 860, 828, 740, 632, 538, 450	13.82 s (1H)	11.81 s (1H)	6.20 s (1H)	5.09 d.d (1H, J_{ax} 10.4, J_{bx} 2.8)	3.78 pseudo-d (1H, J_{ab} 12.4)	3.04 d.d (1H, J_{ab} 12.4, J_{ax} 10.4)	9.38 s (1H), 7.17–7.22 m (2H), 7.07–7.13 m (3H), 6.90 d.t (1H, *J* 1.3, 7.5), 6.72 d (2H, *J* 8.6)
IIId	212 (2.19), 281 (0.91), 313 (1.14), 376 (0.85)	3420, 3377, 3320, 3300, 3048, 2360, 1682, 1652, 1590, 1567, 1475, 1370, 1290, 833, 765, 743, 638, 550, 485	13.96 s (1H)	11.53 s (1H)	5.88 s (1H)	5.06 d.d (1H, J_{ax} 10.4, J_{bx} 2.8)	3.96 pseudo-d (1H, J_{ab} 12.1)	2.83 d.d (1H, J_{ab} 12.1, J_{ax} 10.4)	8.62 s (1H), 8.42 s (1H), 7.09–7.18 m (3H), 6.87 d.t (1H, *J* 1.3, 7.5), 6.76 d (1H, *J* 2.1),

Table 3. (Contd.)

Comp. no.	UV spectrum, (EtOH), λ_{max}, nm ($\varepsilon \times 10^4$)	IR spectrum (KBr), ν, cm^{-1}	^1H NMR spectrum (DMSO-d_6), δ, ppm (J, Hz)						
			OH	N^3H	N^1H	H^x	H^b	H^a	Ar, R
IIId									6.68 d (1H, *J* 8.6), 6.63 d.d (1H, *J* 2.1, 8.6)
IIIe[a]	216 (2.63), 277 (1.05), 314 (1.23), 374 (1.00)	3362, 2990, 2835, 1670, 1632, 1610, 1590, 1563, 1510, 1457, 1407, 1363, 1240, 1174, 1030, 825, 740, 433	13.97 s (1H)	11.57 s (1H)	6.02 s (1H)	5.20 d.d (1H, J_{ax} 9.6, J_{bx} 3.2)	3.92 pseudo-d (1H, J_{ab} 11.8)	2.93 d.d (1H, J_{ab} 11.8, J_{ax} 9.6)	7.27 d (2H, *J* 8.6), 7.10–7.18 m (3H), 6.89 d.t (1H, *J* 1.6, 7.5), 6.84 d (2H, *J* 8.6), 3.78 s (3H)
IIIf[a]	212 (2.26), 281 (0.94), 314 (1.18), 375 (0.89)	3508, 3440, 3359, 3315, 3276, 2929, 2360, 1675, 1663, 1619, 1694, 1566, 1520, 1480, 1447, 1410, 1368, 1279, 857, 761, 743, 687, 643, 550, 490, 432	13.98 s (1H)	11.58 s (1H)	6.01 s (1H)	5.14 d.d (1H, J_{ax} 9.6, J_{bx} 2.2)	3.90 d.d (1H, J_{ab} 11.8, J_{bx} 2.2)	2.99 d.d (1H, J_{ab} 11.8, J_{ax} 9.6)	8.56 s (1H), 7.11–7.18 m (3H), 6.85–6.90 m (2H), 6.76 d.d (1H, *J* 2.1, 8.6), 6.71 d (1H, *J* 8.6), 3.79 s (3H)
IIIg	205 (2.31), 237 (1.55), 313 (1.38), 367 (0.87)	3370, 3354, 3250, 3140, 3028, 2980, 2928, 2867, 2848, 1665, 1594, 1567, 1486, 1447, 1405, 1369, 1240, 1117, 1042, 923, 869, 845, 749, 636, 455	13.77 s (1H)	11.84 s (1H)	6.26 s (1H)	5.12 d.d (1H, J_{ax} 10.0, J_{bx} 2.8)	3.74 pseudo-d (1H, J_{ab} 13.0)	3.11 d.d (1H, J_{ab} 13.0, J_{ax} 10.0)	7.21 t (2H, *J* 8.0), 7.10 d (1H, *J* 8.0), 6.92 d.t (1H, *J* 1.3, 7.5), 6.87 d (1H, *J* 8.0), 6.82 d (1H, *J* 2.0), 6.79 d.d (1H, *J* 2.0, 8.0), 5.98 s (2H)
IIIh	208 (2.39), 262 (1.78), 312 (1.09), 379 (0.74)	3368, 3155, 3030, 2895, 2810, 1693, 1660, 1605, 1560, 1524, 1492, 1450, 1412, 1362, 1337, 1311, 1265, 1160, 810, 752, 618, 542, 453, 430	13.96 s (1H)	11.55 s (1H)	5.88 s (1H)	5.13 d.d (1H, J_{ax} 10.7, J_{bx} 3.2)	3.95 pseudo-d (1H, J_{ab} 12.9)	2.86 d.d (1H, J_{ab} 12.9, J_{ax} 10.7)	7.08–7.19 m (5H), 6.88 d.t (1H, *J* 1.3, 7.5), 6.65 d (2H, *J* 8.6), 2.92 s (6H)
IIIi	213 (2.45), 241 (1.38), 312 (1.23), 366 (0.81)	3375, 3350, 2995, 2850, 2365, 1670, 1633, 1610, 1590, 1560, 1459, 1408, 1365, 1336, 1088, 847, 820, 740, 632, 531, 420	13.80 s (1H)	11.83 s (1H)	6.36 s (1H)	5.23 d.d (1H, J_{ax} 10.0, J_{bx} 2.2)	3.68 d.d (1H, J_{ab} 12.5, J_{bx} 2.2)	3.23 d.d (1H, J_{ab} 12.5, J_{ax} 10.0)	7.40 d (2H, *J* 8.1), 7.33 d (2H, *J* 8.1), 7.20–7.24 m (2H), 7.12 d (1H, *J* 8.1), 6.92 d.t (1H, *J* 1.3, 7.5)

Table 3. (Contd.)

Comp. no.	UV spectrum, (EtOH), λ_{max}, nm ($\varepsilon \times 10^4$)	IR spectrum (KBr), ν, cm^{-1}	^1H NMR spectrum (DMSO-d_6), δ, ppm (J, Hz)						
			OH	N^3H	N^1H	H^x	H^b	H^a	Ar, R
IIIj[a]	216 (2.71), 239 (1.52), 278 (0.78), 317 (1.10), 374 (0.96)	3361, 3154, 3041, 1676, 1642, 1610, 1593, 1570, 1492, 1457, 1403, 1363, 1337, 1302, 1056, 873, 752, 727, 677, 637, 562, 462, 447	14.05 s (1H)	11.48 s (1H)	6.09 d (1H, *J* 2.1)	5.63–5.67 m (1H)	3.54 d.d (1H, J_{ab} 12.9, J_{bx} 3.2)	3.83 d.d (1H, J_{ab} 12.9, J_{ax} 7.5)	7.51–7.55 m (1H), 7.34–7.39 m (1H), 7.23–7.28 m (2H), 7.13–7.18 m (2H), 7.04 d (1H, *J* 8.6), 6.94 d.t (1H, *J* 1.2, 7.5)
IIIk	205 (2.66), 219 (2.54), 237 (2.48), 276 (1.57), 314 (1.72), 376 (1.59)	3440, 3356, 3175, 3050, 2928, 2810, 2238, 1664, 1600, 1570, 1486, 1445, 1408, 1365, 1294, 850, 830, 745, 674, 632, 526, 478, 423	13.78 s (1H)	11.85 s (1H)	6.48 s (1H)	5.34 d.d (1H, J_{ax} 9.6, J_{bx} 3.2)	3.63 pseudo-d (1H, J_{ab} 12.9)	3.40 d.d (1H, J_{ab} 12.9, J_{ax} 9.6)	8.83 d (2H, *J* 8.6), 7.52 d (2H, *J* 8.6), 7.24 t (2H, *J* 8.6), 7.12 d (1H, *J* 8.6), 6.95 t (1H, *J* 7.3)
IIIl	207 (2.76), 214 (2.59), 244 (2.01), 269 (2.02), 315 (1.35), 376 (1.11)	3372, 3150, 2990, 2850, 1666, 1634, 1610, 1590, 1665, 1515, 1485, 1460, 1410, 1343, 1295, 854, 749, 694, 653, 631, 619, 565, 472	13.98 s (1H)	11.62 s (1H)	6.33 s (1H)	5.41 d.d (1H, J_{ax} 10.0, J_{bx} 2.0)	3.82 d.d (1H, J_{ab} 13.0, J_{bx} 2.0)	3.19 d.d (1H, J_{ab} 13.0, J_{ax} 10.0)	8.18 d (2H, *J* 9.0), 7.64 d (2H, *J* 9.0), 7.14–7.22 m (3H), 6.93 d.t (1H, *J* 1.6, 7.0)
IIIm	205 (2.14), 214 (1.91), 272 (0.61), 316 (0.89), 363 (0.93)	3325, 3150, 3015, 1670, 1640, 1608, 1594, 1565, 1481, 1456, 1410, 1364, 1340, 1141, 1005, 836, 745, 640, 596, 549, 461, 435	13.91 s (1H)	11.65 s (1H)	5.83 s (1H)	5.26 d.d (1H, J_{ax} 10.6, J_{bx} 3.7)	3.96 d.d (1H, J_{ab} 12.3, J_{bx} 3.7)	2.97 d.d (1H, J_{ab} 12.3, J_{ax} 10.6)	7.42 s (1H), 7.13–7.19 m (2H), 7.05 d.d (1H, *J* 1.2, 8.1), 6.97 d.t (1H, *J* 1.3, 7.6), 6.31–6.33 m (1H), 6.26 d (1H, *J* 3.5)
IIIn	205 (2.59), 220 (2.35), 249 (1.24), 312 (0.98), 371 (0.86)	3369, 3358, 3305, 3130, 2990, 2845, 1639, 1609, 1593, 1561, 1458, 1408, 1362, 1342, 1291, 1108, 1061, 837, 743, 691, 668, 637, 550, 461, 446, 432	14.05 s (1H)	11.59 s (1H)	5.83 s (1H)	5.54 d.d (1H, J_{ax} 10.4, J_{bx} 2.9)	4.29 pseudo-d (1H, J_{ab} 12.4)	2.89 d.d (1H, J_{ab} 12.4, J_{ax} 10.4)	10.80 s (1H), 7.63 d (1H, *J* 8.6), 7.34 d (1H, *J* 8.6), 7.23 d (1H, *J* 3.2), 7.13–7.20 m (3H), 7.09 t (1H, *J* 7.5), 6.95 d (1H, *J* 7.5), 6.92 d.t (1H, *J* 1.6, 7.5)

Table 3. (Contd.)

Comp. no.	UV spectrum, (EtOH), λ_{max}, nm ($\varepsilon \times 10^4$)	IR spectrum (KBr), ν, cm^{-1}	^1H NMR spectrum (DMSO-d_6), δ, ppm (J, Hz)						
			OH	N^3H	N^1H	H^x	H^b	H^a	Ar, R
IIIo	216 (2.72), 238 (2.26), 275 (1.79), 314 (2.09), 365 (1.88)	3340, 3130, 2988, 2909, 2875, 2850, 1681, 1607, 1590, 1562, 1483, 1462, 1408, 1367, 1340, 1284, 962, 865, 851, 758, 750, 720, 640, 567, 461, 438	13.82 s (1H)	11.87 s (1H)	5.88 s (1H)	4.50–4.56 m (1H)	3.55 d.d (1H, J_{ab} 12.9, J_{bx} 3.2)	2.89 d.d (1H, J_{ab} 12.9, J_{ax} 9.6)	7.17 t (2H, J 7.3), 7.05 d (1H, J 8.1), 6.89 d.t (1H, J 1.2, 7.3), 5.64 d.q (1H, J 15.0, 6.9), 5.52 d.d (1H, J 6.9, 15.0), 1.64 d (3H, J 6.9)
IIIp[a]	208 (2.55), 248 (1.95), 314 (0.74), 365 (0.67)	3370, 3337, 3318, 3023, 2827, 1685, 1610, 1594, 1557, 1470, 1452, 1406, 1353, 1339, 1282, 967, 821, 747, 693, 637, 483, 425	14.01 s (1H)	11.57 s (1H)	5.83 s (1H)	4.81–4.87 m (1H)	3.67 d.d (1H, J_{ab} 12.4, J_{bx} 3.1)	3.12 d.d (1H, J_{ab} 12.4, J_{ax} 10.6)	7.37 d (2H, J 7.5), 7.38 t (2H, J 7.5), 7.19 t (1H, J 7.5), 7.10–7.17 m (3H), 6.91 d.t (1H, J 1.3, 7.5), 6.62 d (1H, J 16.1), 6.31 d.d (1H, J 6.4, 16.1)
IIIq	215 (2.53), 269 (2.76), 312 (1.69), 367 (1.31)	3450, 3356, 3172, 3053, 2836, 1669, 1569, 1470, 1415, 1369, 1327, 1282, 1115, 1012, 958, 882, 810, 745, 426	13.85 s (1H)	11.89 s (1H)	6.10 s (1H)	4.73–4.79 m (1H)	3.51 d.d (1H, J_{ab} 12.6, J_{bx} 2.9)	3.21 d.d (1H, J_{ab} 12.6, J_{ax} 9.1)	7.61 s (1H), 7.19 t (2H, J 7.5), 7.09 d (1H, J 8.1), 6.92 d.t (1H, J 1.3, 8.1), 6.42–6.48 m (3H), 6.15 d.d (1H, J 6.9, 16.1)
IIIr	217 (2.18), 237 (1.67), 282 (1.21), 314 (1.66), 374 (1.16)	3395, 3155, 2967, 2875, 2360, 2340, 1668, 1634, 1610, 1592, 1575, 1465, 1408, 1370, 1333, 1263, 867, 832, 740, 547, 482, 427	14.07 s (1H)	11.49 s (1H)	5.38 s (1H)	3.88 d.d (1H, J 2.7, 4.3, 10.3)	4.04 pseudo-d (1H, J_{ab} 12.0)	2.38 d.d (1H, J_{ab} 12.0, J_{ax} 10.3)	6.99–7.09 m (3H), 6.79 d.t (1H, J 1.3, 7.5), 1.91 m (1H), 1.02 d (3H, J 6.4), 0.94 d (3H, J 6.4)
IIIs	205 (2.69), 215 (1.92), 237 (1.45), 312 (1.24), 359 (0.93)	3450, 3314, 3160, 3055, 3034, 2985, 2955, 2925, 1674, 1655, 1613, 1590, 1561, 1455, 1355, 1335, 1287, 1248, 1161, 836, 766, 709, 600, 486, 438	14.08 s (1H)	11.89 s (1H)	5.59 s (1H)	–	3.28 s (2H)		7.16–7.21 m (2H), 6.98 d (1H, J 8.1), 6.92 d.t (1H, J 1.2, 8.1), 1.27 s (6H)

Table 3. (Contd.)

Comp. no.	UV spectrum, (EtOH), λ_{max}, nm ($\varepsilon \times 10^4$)	IR spectrum (KBr), ν, cm^{-1}	^1H NMR spectrum (DMSO-d_6), δ, ppm (J, Hz)						
			OH	N^3H	N^1H	H^x	H^b	H^a	Ar, R
IIIt	212 (2.39), 276 (1.43), 313 (0.98), 362 (0.72)	3366, 2927, 2848, 2363, 2340, 1693, 1630, 1604, 1571, 1483, 1459, 1398, 1369, 1298, 1259, 868, 842, 750, 640, 631, 542, 485, 445	14.04 s (1H)	11.85 s (1H)	5.54 s (1H)	–	3.33 s (2H)		7.15–7.22 m (2H), 7.08 d (1H, *J* 8.1), 6.91 d.t (1H, *J* 1.2, 8.1), 1.26–1.69 m (10H)
IV	208 (2.69), 218 (2.70), 259 (3.79), 305 (1.95), 406 (1.48)	3450, 3160, 3030, 1668, 1616, 1588, 1570, 1455, 1345, 1248, 1070, 887, 834, 766, 730, 695, 558, 533, 476, 440	14.31 s (1H)	11.92 s (1H)	9.86 s (1H)				8.89 d (2H, *J* 8.4), 8.83 s (1H), 8.18 d (2H, *J* 6.9), 7.75 d.d (1H, *J* 1.2, 7.9), 7.54–7.65 m (6H), 7.48 d.t (1H, *J* 1.2, 7.5), 2.51 s (3H)
V	216 (1.14), 247 (1.13)	3450, 3258, 3099, 3029, 2362, 1684, 1625, 1608, 1599, 1589	–	–	7.84 d.d.d (1H, *J* 1.8, 8.3, 14.8), 7.61–7.67 m (3H), 7.35–7.42 m (3H), 7.27–7.34 m (2H)				
V[b]	340–391 (1.18–1.14), 411 (0.88), 432	1423, 1401, 1315, 1302, 1279, 1003, 952, 905, 888, 777, 750, 725, 685, 640, 613, 549, 505, 451	17.07 s (1H)	8.26 br.s (1H)	7.92 d.d (1H, *J* 9.8, 14.6), 7.74 d (1H, *J* 14.6), 7.53 d.d (2H, *J* 1.8, 8.0), 7.36–7.42 m (3H), 7.09–7.16 m (2H)				

[a] In DMSO-d_6–CCl_4, 1:1. [b] In $CDCl_3$.

compound **II** is characterized by three strong absorption bands at λ 210, 234, and 301 nm, and it shows no fluorescence.

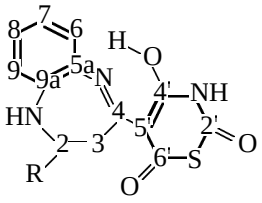
Thus we have developed a new efficient preparative procedure for the synthesis of 4-hydroxy-5-(2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-2*H*-1,3-thiazin-2,6-diones **IIIa**–**IIIt** from readily accessible starting compounds.

EXPERIMENTAL

The UV spectra were recorded from solutions in 96.5% ethanol on an SF-2000 spectrophotometer. The ^1H and ^{13}C NMR spectra were measured on a Bruker AM-500 spectrometer (500 and 125 MHz, respectively) using DMSO-d_6 as solvent. The IR spectra were obtained from samples prepared as KBr pellets on an FSM-1201 Fourier spectrometer. The mass spectra (electron impact, 70 eV) were run on an MKh-1320 instrument. The progress of reactions and the purity of products were monitored by TLC on Sorbfil plates using acetone–hexane (1:2) as eluent.

5-Acetyl-4-hydroxy-3,6-dihydro-2*H*-1,3-thiazine-2,6-dione (I) was synthesized by the procedure described in [1–3]. Acetic anhydride, 45 ml, was added to a solution of 21 g of malonic acid in 100 ml of acetic acid. The mixture was stirred for 15 min at 20–25°C, 19 g of potassium thiocyanate was added in one portion, and the mixture was stirred for 1 h at 20–25°C. The resulting yellow transparent solution was left to stand for 48 h at ~20°C, and the mixture crystallized. It was diluted with 300 ml of water, and the crystals were filtered off, dried in air, and recrystallized from benzene. It is advisable to use a Soxhlet

Table 4. ^{13}C NMR spectra (δ_C, ppm) of 4-hydroxy-5-(2-R-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-2*H*-1,3-thiazine-2,6-diones **IIIa**–**IIIt**, 4-hydroxy-5-{1-*N*-[2-(9-anthrylmethylideneamino)phenyl]ethanimidoyl}-2*H*-1,3-thiazine-2,6-dione (**IV**), and 4-hydroxy-5-[(2*E*,4*E*)-5-phenylpenta-2,4-dienoyl]-2*H*-1,3-thiazine-2,6-dione (**V**)



Comp. no.	C^2	C^3	C^4	$C^{2'}$	$C^{4'}$	$C^{5'}$	$C^{6'}$	C^{5a}, C^6, C^7, C^8, C^9, C^{9a}	R
II		20.1	180.3	174.9	168.4	97.9	163.1	143.8, 129.3, 126.9, 120.2, 116.1, 115.8	
IIIa	66.3	37.4	180.8	170.2	167.8	97.1	162.8	141.4, 128.6, 124.8, 124.4, 120.9, 119.8	144.5, 128.3, 127.5, 125.6
IIIb	66.1	37.5	180.8	170.2	167.8	97.1	162.8	141.3, 128.5, 125.5, 124.4, 120.9, 119.8	141.6, 136.6, 128.8, 124.8, 20.5
IIIc	65.5	37.7	180.7	170.3	167.8	96.9	162.8	141.3, 128.5, 124.8, 124.2, 120.9, 119.6	156.7, 135.1, 126.7, 114.9
IIId	66.7	37.9	181.2	170.2	167.7	96.9	162.6	141.4, 128.1, 124.3, 124.1, 121.3, 119.5	144.9, 144.6, 136.1, 116.2, 115.2, 113.0
IIIe	65.8	37.6	180.8	170.3	167.8	97.1	162.8	141.3, 128.5, 126.8, 124.8, 120.9, 119.7	158.6, 136.7, 126.8, 113.7, 55.1
IIIf	66.55	37.7	181.1	170.2	167.9	96.9	162.6	141.4, 128.1, 124.4, 124.2, 121.1, 119.6	147.2, 146.1, 135.6, 117.9, 115.1, 109.8, 55.4
IIIg	66.3	37.6	181.0	170.3	167.9	97.3	163.1	141.4, 128.8, 125.0, 124.5, 121.1, 119.1	147.3, 146.7, 138.7, 120.1, 108.1, 106.3, 101.1
IIIh	66.1	37.8	180.7	170.3	167.8	97.1	162.9	141.4, 128.4, 124.8, 124.1, 121.1, 119.6	149.9, 132.4, 126.2, 112.2, 40.1
IIIi	66.0	37.2	181.2	169.8	167.8	97.0	162.5	141.1, 128.2, 124.8, 124.3, 121.3, 120.0	143.3, 132.3, 128.0, 127.3
IIIj	63.7	33.6	180.3	169.8	167.5	97.3	162.7	140.2, 128.6, 124.9, 124.4, 120.7, 119.9	141.4, 131.2, 129.2, 129.1, 127.8, 126.9
IIIk	65.96	36.4	180.8	169.8	167.7	97.2	162.8	141.1, 128.7, 125.0, 124.6, 120.9, 118.7	149.5, 132.3, 126.9, 120.2, 110.2
IIIl	65.8	36.3	180.8	169.7	167.6	97.2	162.7	141.0, 128.7, 127.2, 125.0, 123.5, 120.3	151.5, 146.7, 124.7, 120.9
IIIm	60.8	34.7	180.7	170.3	167.7	97.2	162.9	140.5, 128.4, 126.2, 124.4, 122.0, 121.2	155.5, 142.1, 110.2, 105.5
IIIn	60.6	37.3	180.9	170.7	167.8	97.1	162.9	141.4, 128.5, 124.9, 124.6, 121.2, 120.1	136.2, 124.8, 121.9, 121.4, 119.0, 118.9, 118.6, 111.5
IIIo	64.9	35.6	180.7	170.9	167.9	96.9	162.9	140.8, 128.3, 125.3, 124.6, 121.3, 120.1	132.6, 124.8, 17.2
IIIp	65.4	35.2	180.8	170.8	167.9	97.1	162.9	140.8, 128.4, 124.9, 124.7, 121.4, 120.2	136.2, 130.9, 129.2, 128.5, 127.6, 126.3
IIIq	64.7	35.2	180.8	170.6	167.8	97.1	162.9	140.7, 128.4, 124.8, 124.7, 121.3, 120.2	151.5, 142.7, 128.9, 118.1, 111.6, 108.8
IIIr	68.4	35.0	181.1	171.9	168.0	96.7	162.5	141.4, 127.8, 124.3, 123.9, 121.0, 119.1	31.3, 18.4, 17.1

Table 4. (Contd.)

Comp. no.	C^2	C^3	C^4	$C^{2'}$	$C^{4'}$	$C^{5'}$	$C^{6'}$	C^{5a}, C^6, C^7, C^8, C^9, C^{9a}	R
IIIs	66.3	39.5	180.9	170.6	168.3	97.3	162.8	140.7, 128.4, 125.4, 124.4, 121.2, 120.2	29.6
IIIt	67.3	38.3	180.8	170.5	168.1	97.5	162.8	140.3, 128.2, 125.5, 124.4, 121.9, 120.1	37.6, 25.1, 21.2
IV		21.0	180.3	173.7	168.3	97.5	162.9	162.3, 147.5, 131.6, 130.7, 130.2, 130.0, 129.7, 129.0, 127.5, 127.1, 126.98, 125.8, 125.6, 124.7, 119.9	
V			183.9	180.7	173.3	99.6	163.0	148.9, 144.9, 135.6, 129.87, 128.86, 127.89, 127.4, 123.79	

extractor for recrystallization. Yield 25 g (46%), mp 198–200°C.

5-[*N*-(2-Aminophenyl)ethanimidoyl]-4-hydroxy-2*H*-1,3-thiazine-2,6-dione (II). A mixture of 1 g of finely powdered 5-acetyl-4-hydroxy-1,3-thiazine-2,6-dione **I** 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 (in 1–2 min after the mixture became boiling), almost colorless fine needle-shaped crystals began to quickly separate from the solution. After cooling, the crystals were filtered off, washed with propan-2-ol, and dried in air. The product was analytically pure, and no additional purification was necessary. 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 IIIa–IIIt *(general procedure). a*. Trifluoroacetic acid, 5–7 drops, was added to a mixture of 1 g of compound **II** 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 initial compound **II** disappeared completely. During the process, poorly soluble compound **II** was gradually converted into poorly soluble product which was as a rule a yellow finely crystalline powder. In some cases, e.g., in the reaction with vanillin, the reactants dissolved completely during the first 15 min, and only then product **IIIf** began to crystallize from the solution. The mixture was cooled, and the crystals were filtered off and washed with 2–3 portions of propan-1-ol. As a rule, the product was analytically pure, and no additional purification was required. If necessary, benzodiaxepines **III** can be recrystallized from dioxane (however, the solvent is difficult to remove from the substance; the recrystallized product should be dried under reduced pressure on heating). Compound **IIIj** obtained from *o*-chlorobenzaldehyde is readily soluble in propan-1-ol; therefore, when the reaction was complete, 2/3 of the solvent was removed under reduced pressure, and the product was then isolated following the general procedure. In the synthesis of compounds **IIIs** and **IIIt** we used a large excess of acetone and cyclohexanone, respectively (3 ml per gram of **II**).

b. A mixture of 1 g of 5-acetyl-4-hydroxy-1,3-thiazine-2,6-dione (**I**) and 580 mg of *o*-phenylenediamine in 20 ml of propan-1-ol was heated for 5 min under reflux. The mixture was cooled, 1.5–2 equiv of the corresponding aldehyde and 5–7 drops of trifluoroacetic acid were added, and the mixture was heated for 1.5–2 h under reflux and was then treated as described above in *a*. The yields of the products obtained by methods *a* and *b* were almost similar.

4-Hydroxy-5-[2-(4-nitrophenyl)-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl]-2*H*-1,3-thiazine-2,6-dione (IIIl). A mixture of 1 g of compound **II** and 600 mg of 4-nitrobenzaldehyde in 15 ml of acetic acid was heated for 1 h under reflux. The solvent was removed on a rotary evaporator, 7 ml of ethanol was added to the residue, and the mixture was heated to the boiling point. After cooling, the crystals were filtered off. washed with 2–3 small portions of ethanol, and dried in air. Yield 725 mg (49%), mp 257–258°C (decomp).

5-[2-(4-Chlorophenyl)-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl]-4-hydroxy-2*H*-1,3-thiazine-2,6-dione (IIIi), 5-[2-(4-cyanophenyl)-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl]-4-hydroxy-2*H*-1,3-thiazine-2,6-dione (IIIk), and 4-hydroxy-5-(2-isopropyl-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-2*H*-1,3-thiazine-2,6-dione (IIIr) were synthesized as described above for compound **IIIl**.

4-Hydroxy-5-[(2*E*,4*E*)-5-phenylpenta-2,4-dienoyl]-2*H*-1,3-thiazine-2,6-dione (V). Pyridine, 5 drops, and piperidine, 5 drops, were added to a mixture of 1 g of 5-acetyl-4-hydroxy-1,3-thiazine-2,6-dione (**I**) and 0.7 ml of cinnamaldehyde in 15 ml of chloroform. The mixture was heated for 2 h

under reflux and cooled, and the orange plates were filtered off, washed with a small amount of chloroform, and dried in air. Yield 1.2 g (74%), mp 215–216°C (decomp.)

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