Studies on Quinolizine Derivatives. XXIII.[1] Synthesis and Reactions of Methylthioazacycl[3.3.3]-azines

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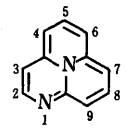
Dimethyl 7-acyl-9-cyano-1-azacycl[3.3.3]azine-2,3-dicarboxylates (4, 6) were synthesized *via* 1-acyl-3-cyano-4-imino-4*H*-quinolizines (3, 5) as key intermediates. The nucleophilic substitution of the methylthio group in antiaromatic azacycl[3.3.3]azines (6b, 9, 13) gave the corresponding products. The reaction of 9 or 13 with methyl acetoacetate gave the fused diazacycl[3.3.3]azines (12, 16), which are examples of a new ring system.

Keywords azacycl[3.3.3]azine; nucleophilic substitution; fused diazacycl[3.3.3]azine; ^{1}H-NMR spectra; steric hindrance

The azacycl[3.3.3]azines have been the subject of numerous theoretical and synthetic investigations.[2] Our earlier papers have presented syntheses and reactions of various azacycl[3.3.3]azines (**1**), heterocyclic [12]annulenes.[2b,3] In this paper, we wish to report the synthesis of dimethyl 7-acyl-9-cyano-8-methylthio-1-azacycl[3.3.3]azine-2,3-dicarboxylate (**6**), and the nucleophilic substitution of its methylthio group to investigate in more detail some of the features noted in the antiaromatic azacycl[3.3.3]azines.



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The reaction of 2-acylmethylpyridines (**2**) and ethoxymethylenemalononitrile (EMN) with K_2CO_3 in dimethylsulfoxide (DMSO) gave 4-imino-4*H*-quinolizines (**3**) in good yields. Cyclization of **3** with dimethyl acetylenedicarboxylate (DMAD) in dimethylformamide (DMF) at 130 °C gave the corresponding 1-azacycl[3.3.3]azines (**4**). In a similar manner, 8-methylthioazacyclazines (**6**) were synthesized by the reaction of 2-methylthio-4-imino-4*H*-quinolizines (**5**), which were prepared from **2** and 3,3-bismethylthio-2-cyanoacrylonitrile (BAN). Next, we attempted the nucleophilic substitution of **6b**. Compound **6b** reacted with benzylamine, diethyl malonate, and methyl acetoacetate to give the corresponding substituted products (**7**, **8**) in good yields.

In the proton nuclear magnetic resonance (^{1}H-NMR) spectra, the signals due to C_6-H of **4a** and **4b** appear at δ (ppm): 7.90 and 7.32, while those due to C_6-H of **6**, **7**, and **8** appear at δ: 5.27—5.71. Namely, the introduction of the substituent at C_8 caused the signals of C_6-H of **6**, **7**, and **8** to be shifted to higher magnetic fields than those of C_6-H of **4**. In conjugated systems, steric repulsion between substituent groups opposes conjugation as seen in a series of acetophenones, in which there is a torsional angle between the phenyl and carbonyl bonding planes.[4] On this basis, steric repulsions among the three substituent groups attached to

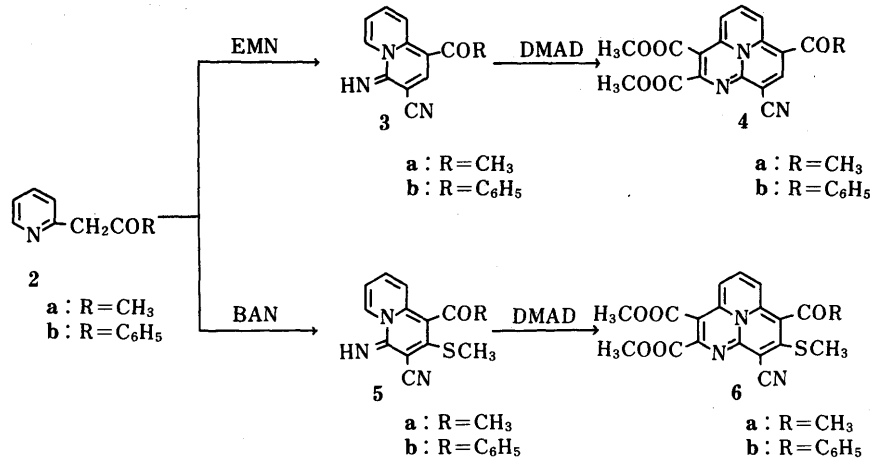

Chart 1

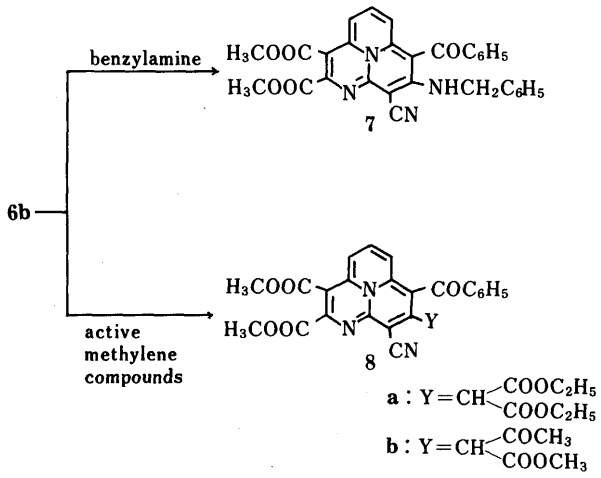

Chart 2

the azacyclazine ring in **6**, **7**, and **8** may oppose conjugation between the azacyclazine ring and the carbonyl group, and cancel the downfield shift of C_6-H. We consider that the signals of C_6-H of **6**, **7**, and **8** appear at δ: 5.27—5.71 due to the anisotropy.[2b,5]

Previously, we reported that methylthiodiazacyclazine derivatives (**9**, **13**) reacted with morpholine to give the substituted products.[6] In this paper, the nucleophilic substitution of the diazacyclazines (**9**, **13**) with various nucleophilic reagents, such as primary amines (benzylamine, ethanolamine) or active methylene compounds (dimethyl

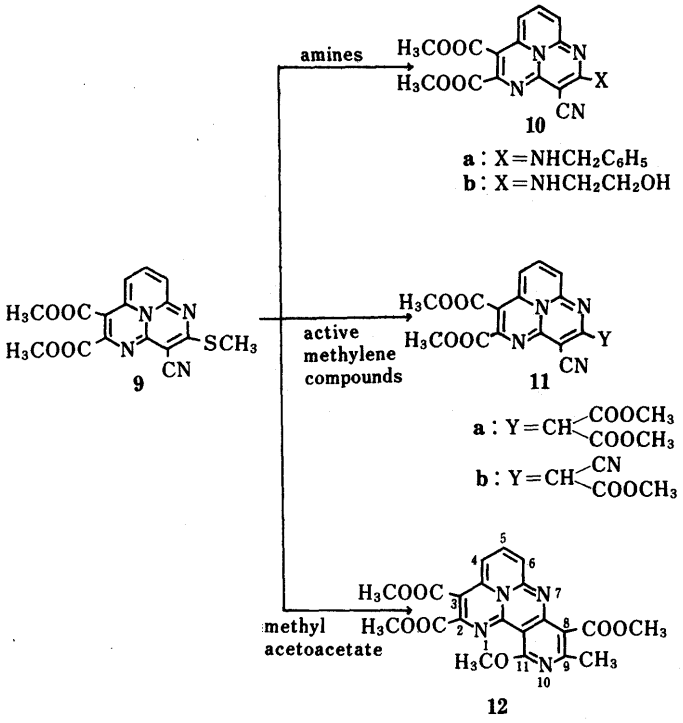

Chart 3

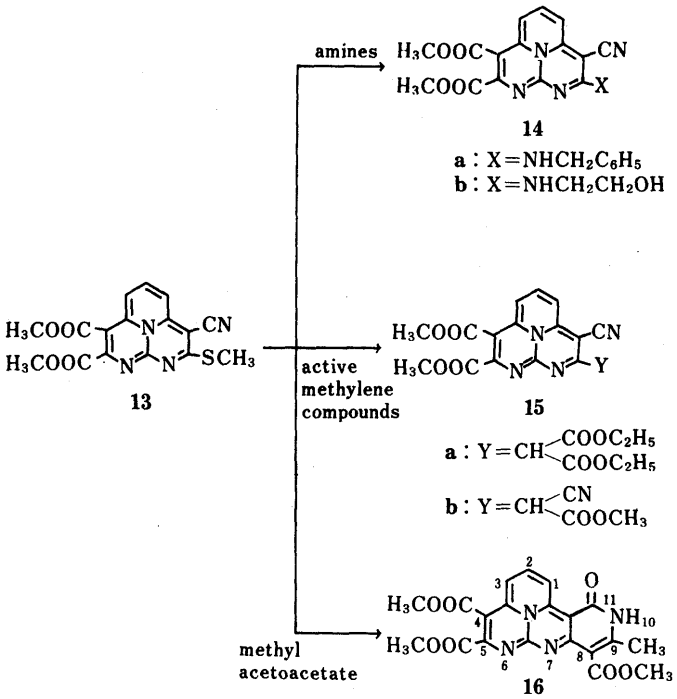

Chart 4

TABLE I. Analytical Data for **4**, **6**, **7**, and **8**

No.	mp (°C)	Yield (%)	Formula	Analysis (%) Calcd C	H	N	Found C	H	N
4a	260	20	$C_{18}H_{13}N_3O_5$	61.54	3.73	11.96	61.64	3.68	11.99
4b	237	21	$C_{23}H_{15}N_3O_5$	66.83	3.66	10.17	66.85	3.60	10.21
6a	285	22	$C_{19}H_{15}N_3O_5S$	57.42	3.80	10.57	57.72	4.02	10.39
6b	272	20	$C_{24}H_{17}N_3O_5S$	62.74	3.73	9.15	62.61	3.75	9.00
7	274	77	$C_{30}H_{22}N_4O_5$	69.49	4.28	10.81	69.61	4.43	10.79
8a	172	75	$C_{30}H_{25}N_3O_9$	63.05	4.41	7.35	63.14	4.39	7.28
8b	234	83	$C_{28}H_{21}N_3O_8$	63.76	4.01	7.97	63.77	4.08	7.87

TABLE II. Spectral Data for **4**, **6**, **7**, and **8**

No.	IR (KBr) cm^{-1}	UV λ_{max}^{EtOH} nm (log ε)	^{1}H-NMR (ppm) C_4-H	C_5-H	C_6-H	C_8-H	Others
4a	2200 (CN), 1740 (C=O), 1710 (C=O), 1625 (C=O)	273 sh,[a] 285, 374, 412 sh, 444, 470	6.57 (dd)	6.85 (t)	7.90 (dd)	7.02 (s)	2.19 (3H, s, CH_3),[b] 3.69 (3H, s, OCH_3), 3.78 (3H, s, OCH_3)
4b	2200 (CN), 1730 (C=O), 1710 (C=O), 1640 (C=O)	273 (4.45), 287 (4.41) sh, 376 (4.07), 450 (4.38), 476 (4.59)	6.58 (dd)	6.78 (t)	7.32 (dd)	6.60 (s)	3.68 (3H, s, OCH_3),[b] 3.76 (3H, s, OCH_3), 7.44—7.60 (5H, m, Ar-H)
6a	2200 (CN), 1740 (C=O), 1700 (C=O), 1610 (C=O)	228 sh,[a] 268, 288 sh, 340, 396, 430, 454	6.56 (dd)	6.46 (t)	5.38 (dd)		2.33 (3H, s, CH_3),[b] 2.43 (3H, s, SCH_3), 3.60 (3H, s, OCH_3), 3.74 (3H, s, OCH_3)
6b	2200 (CN), 1730 (C=O), 1710 (C=O), 1660 (C=O)	269,[a] 295 sh, 346, 396, 432, 456	6.51 (dd)	6.35 (t)	5.27 (dd)		2.27 (3H, s, SCH_3),[b] 3.61 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 7.41—8.08 (5H, m, Ar-H)
7	2210 (CN), 1750 (C=O), 1720 (C=O), 1620 (C=O)	265 (4.61), 339 (4.39), 488 (4.30)	6.69 (dd)	6.51 (t)	5.71 (dd)		3.73 (3H, s, OCH_3),[b] 3.85 (3H, s, OCH_3), 4.86 (2H, d, J=5.5 Hz, CH_2), 7.22—7.54 (8H, m, Ar-H), 7.74—7.85 (2H, m, Ar-H), 8.98 (1H, t, J=5.5 Hz, NH)
8a	2200 (CN), 1750 (C=O), 1740 (C=O), 1700 (C=O), 1660 (C=O), 1610 (C=O)	271 (4.52), 294 (4.38) sh, 390 (4.20), 4.28 (4.31) sh, 454 (4.44)	6.51 (dd)	6.67 (t)	5.30 (dd)		1.10 (6H, t, J=7 Hz, $CH_2\underline{CH_3}\times 2$),[c] 3.55 (3H, s, OCH_3), 3.70 (3H, s, OCH_3), 3.87 (1H, s, CH), 4.03 (4H, q, J=7 Hz, $\underline{CH_2}CH_3\times 2$), 7.56—7.76, 8.13—8.27 (5H, m, Ar-H)
8b	2200 (CN), 1740 (C=O), 1720 (C=O), 1620 (C=O)	270,[a] 291 sh, 289, 433, 457	6.53 (dd)	6.36 (t)	5.44 (dd)		2.02 (3H, s, CH_3),[b] 3.61 (3H, s, OCH_3), 3.63 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 7.44—7.61, 7.82—7.92 (5H, m, Ar-H)

a) Concentration unknown because of poor solubility. *b*) In $CDCl_3$. *c*) In DMSO-d_6. dd=double doublet (J=8, 2 Hz), t=triplet (J=8 Hz), sh=shoulder.

malonate, diethyl malonate, methyl cyanoacetate) was examined. In a similar manner to the preparation of **7** or **8**, the corresponding substituted products (**10**, **11**, **14**, and **15**) were obtained in good yields.

Despite numerous reports on the synthesis of cycl[3.3.3]-azine derivatives, only a few examples of the synthesis of fused cycl[3.3.3]azines have been reported.[7] In the case of the reaction of **9** or **13** with methyl acetoacetate and K_2CO_3 in DMSO, triazabenzocycl[3.3.3]azine derivatives (**12**, **16**), which are examples of a new ring system were obtained. Thus, **9** gave trimethyl 11-methoxy-9-methyl-1,7,10-triazabenzo[*b*]cycl[3.3.3]azine-2,3,8-tricarboxylate (**12**). Its structure was supported by a satisfactory elemental analysis, the absence of CN absorption in the infrared (IR) spectrum, and the signals of five methyl groups in the ^{1}H-NMR spectrum. Compound **12** was formed by the substitution of the methylthio group of **9** with methyl acetoacetate, followed by ring closure between the cyano and acetyl groups during recrystallization from MeOH. Similarly, trimethyl 10,11-dihydro-9-methyl-11-oxo-6,7,10-triazabenzo[*a*]cycl[3.3.3]azine-4,5,8-tricarboxylate (**16**) was obtained from **13**. On the contrary, dimethyl 4-carbamoyl-3-methylthiocycl[3.2.2]azine-1,2-carboxylate (**17**) did not react with amine.[8] These observations suggest that the nitrogen-bridged peripheral 12 π electron system of **6**, **9**, and **13** has antiaromatic character, while the nitrogen-bridged peripheral 10 π electron system of **17** has aromatic character.

TABLE III. Analytical Data for **10**, **11**, and **12**

No.	mp (°C)	Yield (%)	Formula	Analysis (%) Calcd C	H	N	Found C	H	N
10a	224	85	$C_{22}H_{17}N_5O_4$	63.61	4.13	18.86	63.55	4.29	18.89
10b	238	78	$C_{17}H_{15}N_5O_5$	55.28	4.09	18.96	55.33	4.23	18.85
11a	201	76	$C_{20}H_{16}N_4O_8$	54.55	3.66	12.72	54.53	3.75	12.55
11b	261	75	$C_{19}H_{13}N_5O_6$	51.47	3.86	15.80	51.33	3.85	15.67
12	209	80	$C_{21}H_{18}N_4O_7$	57.53	4.14	12.78	57.35	4.23	12.54

Experimental

Melting points were determined with a Mitamura Mel-Temp and are uncorrected. IR spectra were recorded in KBr discs on a JASCO IRA-2 spectrometer. Ultraviolet (UV) spectra were recorded on a Hitachi EP-S2 spectrometer in 95% ethanol. ^{1}H-NMR spectra were obtained on a JNM-FX-90 (90 MHz) spectrometer with tetramethylsilane as an internal standard.

1-Acyl-3-cyano-4-imino-4*H*-quinolizines (3a, b) A solution of **2** (0.01 mol), EMN (0.01 mol), and K_2CO_3 (2 g) in DMSO (20 ml) was stirred overnight at room temperature. The reaction mixture was poured into ice-water (300 ml). The solution was extracted with $CHCl_3$ (3 × 50 ml), dried (Na_2SO_4) and evaporated under reduced pressure. The residue was recrystallized from $CHCl_3$–MeOH to give **3**. **3a** (96%), mp 255 °C. *Anal.* Calcd for $C_{12}H_9N_3O$: C, 68.24; H, 4.29; N, 19.89. Found: C, 67.96; H, 4.44; N, 19.71. UV λ_{max}^{EtOH} nm (log ε): 223 (4.35), 273 (3.97) sh, 284 (4.04), 301 (4.04), 369 (4.13) sh, 375 (4.20), 448 (4.04). IR (KBr) cm^{-1}: 2200 (CN), 1660 (C=O). ^{1}H-NMR δ ($CDCl_3$): 2.50 (3H, s, CH_3), 7.54 (1H, t, J=7 Hz, C_7-H or C_8-H), 8.12 (1H, t, J=7 Hz, C_7-H or C_8-H), 8.39 (1H, s, C_2-H), 9.33 (1H, d, J=7 Hz, C_9-H), 9.61 (1H, d, J=7 Hz, C_6-H), **3b** (70%), mp 166 °C. *Anal.* Calcd for $C_{17}H_{11}N_3O$: C, 74.71; H, 4.06; N, 15.38. Found: C, 74.82; H, 4.29; N, 15.38. UV λ_{max}^{EtOH} nm (log ε): 215 (4.37), 259 (4.02) sh, 276 (3.86), 285 (3,81), 315 (3.79) sh, 382 (4.16) sh, 376 (4.23), 452 (4.05). IR (KBr) cm^{-1}: 2200 (CN), 1650 (C=O). ^{1}H-NMR δ ($CDCl_3$): 7.74 (1H, s, C_2-H), 7.25—7.97 (7H, m, C_7-H, C_8-H, and Ar-H), 9.10 (1H, t, J=9 Hz, C_9-H), 9.74 (1H, t, J=9 Hz, C_6-H).

1-Acyl-3-cyano-4-imino-2-methylthio-4*H*-quinolizines (5a, b) These compounds (**5a, b**) were prepared from **2** (0.01 mol), BAN (0.01 mol) and K_2CO_3 (2 g) in DMSO (20 ml) in a manner similar to that used for the preparation of **3**. **5a** (57%), mp 147 °C. *Anal.* Calcd for $C_{13}H_{11}N_3OS$: C, 60.68; H, 4.31; N, 16.33. Found: C, 60.68; H, 4.40; N, 16.20. UV λ_{max}^{EtOH} nm (log ε): 223 (4.31), 260 (4.09), 285 (3.95) sh, 319 (3.96), 388 (3.82), 474 (4.09). IR (KBr) cm^{-1}: 2200 (CN), 1680 (C=O). ^{1}H-NMR δ ($CDCl_3$): 2.63 (6H, s, SCH_3 and CH_3), 7.03—7.20 (1H, m, C_9-H), 7.55—7.62 (2H, m, C_7-H and C_8-H), 9.47 (1H, t, J=7 Hz, C_6-H). **5b** (96%), mp 168 °C. *Anal.* Calcd for $C_{18}H_{13}N_3OS$: C, 67.69; H, 4.10; N, 13.16. Found: C, 67.44; H, 4.27; N, 12.95. UV λ_{max}^{EtOH} nm (log ε): 229 (4.35) sh, 261 (4.41), 291

TABLE IV. Spectral Data for **10**, **11**, and **12**

No.	IR (KBr) cm^{-1}	UV λ_{max}^{EtOH} nm (log ε)	^{1}H-NMR (ppm) C_7-H, C_9-H	C_8-H	Others
10a	3300 (NH), 2210 (CN), 1750 (C=O), 1700 (C=O)	250,[a] 321, 404, 423	6.25, 6.91 (dd) (dd)	7.12 (t)	3.72 (3H, s, OCH_3),[b] 3.82 (3H, s, OCH_3), 4.57 (2H, d, J=6 Hz, CH_2), 5.66 (1H, br t, NH), 7.19—7.40 (5H, m, Ar-H)
10b	3320 (NH, OH), 2200 (CN), 1740 (C=O), 1700 (C=O)	248 (4.51), 320 (4.48), 380 (3.92) sh, 403 (4.25), 423 (4.30)	6.76, 7.00 (dd) (dd)	7.64 (t)	3.87—4.50 (4H, m, CH_2CH_2),[d] 3.96 (3H, s, OCH_3), 3.97 (3H, s, OCH_3)
11a	2210 (CN), 1725 (C=O), 1620 (C=O)	261 (4.37), 273 (4.35), 355 (4.20), 390 (4.25) sh, 405 (4.36), 427 (4.29)	6.08, 6.55 (dd) (dd)	6.95 (t)	3.70 (3H, s, OCH_3),[b] 3.78 (3H, s, OCH_3), 3.80 (6H, s, OCH_3), 4.43 (1H, s, CH)
11b	2200 (CN), 1735 (C=O), 1630 (C=O)	220,[a] 260 sh, 295, 346, 404	7.05, 7.36 (dd) (dd)	7.84 (t)	3.73 (3H, s, OCH_3),[c] 3.77 (3H, s, OCH_3), 3.82 (3H, s, OCH_3)
12	1745 (C=O), 1730 (C=O), 1710 (C=O), 1640 (C=O)	245 (4.39), 255 (4.34) sh, 275 (4.24) sh, 331 (4.32) sh, 348 (4.45), 366 (4.17) sh, 400 (3.85) sh, 420 (4.03), 442 (4.03), 462 (3.74) sh	5.63, 6.11 (dd) (dd)	6.74 (t)	2.25 (3H, s, CH_3),[b] 3.81 (3H, s, OCH_3), 3.85 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 3.94 (3H, s, OCH_3)

a) Concentration unknown because of poor solubility. *b*) In $CDCl_3$. *c*) In DMSO-d_6. *d*) In $CDCl_3$–F_3CCOOH. dd=double doublet (J=8, 2 Hz), t=triplet (J=8 Hz), sh=shoulder.

TABLE V. Analytical Data for **14**, **15**, and **16**

No.	mp (°C)	Yield (%)	Formula	Analysis (%) Calcd C	H	N	Found C	H	N
14a	248	87	$C_{22}H_{17}N_5O_4$	63.61	4.13	16.86	63.51	4.26	16.78
14b	300>	85	$C_{17}H_{15}N_5O_5$	55.28	4.09	18.96	55.35	4.13	18.88
15a	192	81	$C_{22}H_{20}N_4O_8$	56.41	4.30	11.96	56.37	4.37	11.99
15b	261	76	$C_{19}H_{13}N_5O_6$	56.02	3.22	17.19	56.11	3.17	17.23
16	257	73	$C_{20}H_{16}N_4O_7$	56.61	3.80	13.20	56.54	3.76	13.16

TABLE VI. Spectral Data for **14**, **15**, and **16**

No.	IR (KBr) cm^{-1}	UV λ_{max}^{EtOH} nm (log ε)	^1H-NMR (ppm)			
			C_4-H,	C_6-H	C_5-H	Others
14a	3300 (NH), 2200 (CN), 1750 (C=O), 1710 (C=O)	252 (4.51), 317 (4.42), 414 (3.81), 435 (3.81), 580 (2.67)	6.37, (dd)	6.84 (dd)	7.05 (t)	3.75 (3H, s, OCH_3),[b] 3.82 (3H, s, OCH_3), 4.66 (2H, d, J=5 Hz, CH_2), 5.54 (1H, t, J=5 Hz, NH), 7.24—7.34 (5H, m, Ar-H)
14b	3300 (NH), 2190 (CN), 1735 (C=O), 1705 (C=O)	251,[a] 274 sh, 316, 332 sh, 415, 434, 464 sh	6.32, (dd)	6.78 (dd)	7.23 (t)	3.39—3.48 (4H, m, CH_2CH_2),[c] 3.65 (3H, s, OCH_3), 3.73 (3H, s, OCH_3), 4.63 (1H, br, NH), 7.60 (1H, br, OH)
15a	2200 (CN), 1745 (C=O), 1705 (C=O), 1655 (C=O)	264 (4.32), 332 (4.30) sh, 347 (4.56), 386 (4.18) sh, 409 (4.26), 430 (4.18) sh, 580 (3.48)	7.00, (dd)	7.22 (dd)	7.83 (t)	1.33 (6H, t, J=7 Hz, $OCH_2\underline{CH_3}\times 2$),[d] 3.92 (3H, s, OCH_3), 3.93 (3H, s, OCH_3), 4.34 (4H, q, J=7 Hz, $O\underline{CH_2}CH_3\times 2$)
15b	2200 (CN), 1745 (C=O), 1725 (C=O)	263,[a] 290 sh, 351, 395, 599	6.83, (dd)	7.08 (dd)	7.42 (t)	3.82 (3H, s, OCH_3),[b] 3.88 (3H, s, OCH_3), 3.89 (3H, s, OCH_3)
16	1730 (C=O), 1715 (C=O), 1700 (C=O)	253,[a] 329, 354 sh, 386 sh, 408, 429	7.24, (dd)	7.24 (dd)	8.02 (t)	2.21 (3H, s, CH_3),[b] 3.74 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 3.84 (3H, s, OCH_3)

a) Concentration unknown because of poor solubility. *b*) In $CDCl_3$. *c*) In DMSO-d_6. *d*) In $CDCl_3$–F_3CCOOH. dd=double doublet (J=8, 2 Hz), t=triplet (J=8 Hz), sh=shoulder.

(3.84) sh, 335 (3.89), 394 (3.82), 476 (4.08). IR (KBr) cm^{-1}: 2200 (CN), 1660 (C=O). ^{1}H-NMR δ ($CDCl_3$): 2.47 (3H, s, SCH_3), 9.51 (1H, t, J=7 Hz, C_6-H), 7.0—7.9 (8H, m, C_7-H, C_8-H, C_9-H, and Ar-H).

General Procedure for the Preparation of Dimethyl 1-Azacycl[3.3.3]-azine-2,3-dicarboxylates (4, 6) A solution of **3** or **5** (0.01 mol) and DMAD (0.03 mol) in DMF (10 ml) was heated at 130 °C for 3 h. The reaction mixture was poured into ice-water (300 ml). The solution was extracted with $CHCl_3$ (3×50 ml). The extract was washed with H_2O (50 ml), dried (Na_2SO_4) and evaporated under reduced pressure. The residue was submitted to column chromatography on silica gel. From the benzene fraction, the corresponding 1-azacycl[3.3.3]azine derivatives (**4**, **6**) were obtained. The analytical and spectral data for the products are given in Tables I and II.

Dimethyl 8-Benzylamino-7-benzoyl-9-cyano-1-azacycl[3.3.3]azine-2,3-dicarboxylate (7) A solution of **6b** (0.01 mol) and benzylamine (0.01 mol) in DMF (10 ml) was heated at 100 °C for 3 h. The reaction mixture was poured into ice-water (300 ml). The precipitate was filtered off, washed with H_2O, and air-dried to afford **7**. The analytical and spectral data for the product are given in Tables I and II.

Dimethyl 7-Benzoyl-9-cyano-8-[di(ethoxycarbonyl)methyl]-1-azacycl-[3.3.3]azine-2,3-dicarboxylate (8a) A solution of **6b** (0.01 mol), diethyl malonate (0.01 mol) and K_2CO_3 (2 g) in DMSO (20 ml) was stirred at room temperature for 24 h. The reaction mixture was poured into ice-water (300 ml). The precipitate was filtered off, washed with H_2O, and air-dried to afford **8a**. The analytical and spectral data for the product are given in Tables I and II.

Dimethyl 8-(1-Acetyl-1-methoxycarbonylmethyl)-7-benzoyl-9-cyano-1-azacycl[3.3.3]azine-2,3-dicarboxylate (8b) Compound **8b** was prepared from **6b** in a manner similar to that used for the preparation of **8a**. The analytical and spectral data for the product are given in Tables I and II.

Dimethyl 2-Benzylamino-3-cyano-1,4-diazacycl[3.3.3]azine-5,6-dicarboxylate (10a) Compound **10a** was prepared from **9** in a manner similar to that used for the preparation of **7**. The analytical and spectral data for the product are given in Tables III and IV.

Dimethyl 3-Cyano-2-(2-hydroxyethylamino)-1,4-diazacycl[3.3.3]azine-5,6-dicarboxylate (10b) Compound **10b** was prepared from **9** in a manner similar to that used for the preparation of **7**. The analytical and spectral data for the product are given in Tables III and IV.

Dimethyl 3-Cyano-2-[di(methoxycarbonyl)methyl]-1,4-diazacycl[3.3.3]-azine-5,6-dicarboxylate (11a) Compound **11a** was prepared from **9** in a manner similar to that used for the preparation of **8**. The analytical and spectral data for the product are given in Tables III and IV.

Dimethyl 3-Cyano-2-(1-cyano-1-methoxycarbonylmethyl)-1,4-diazacycl-[3.3.3]azine-5,6-dicarboxylate (11b) Compound **11b** was prepared from **9** in a manner similar to that used for the preparation of **8**. The analytical and spectral data for the product are given in Tables III and IV.

Trimethyl 11-Methoxy-9-methyl-1,7,10-triazabenzo[*b*]cycl[3.3.3]-azine-2,3,8-tricarboxylate (12) Compound **12** was prepared from **9** in a manner similar to that used for the preparation of **8**. The analytical and spectral data for the product are given in Tables III and IV.

Dimethyl 8-Benzylamino-7-cyano-1,9-diazacycl[3.3.3]azine-2,3-dicarboxylate (14a) Compound **14a** was prepared from **13** in a manner similar to that used for the preparation of **7**. The analytical and spectral data for the product are given in Tables V and VI.

Dimethyl 7-Cyano-8-(2-hydroxyethylamino)-1,9-diazacycl[3.3.3]azine-2,3-dicarboxylate (14b) Compound **14b** was prepared from **13** in a manner similar to that used for the preparation of **7**. The analytical and spectral data for the product are given in Tables V and VI.

Dimethyl 7-Cyano-8-[di(ethoxycarbonyl)methyl]-1,9-diazacycl[3.3.3]-azine-2,3-dicarboxylate (15a) Compound **15a** was prepared from **13** in a manner similar to that used for the preparation of **8**. The analytical and spectral data for the product are given in Tables V and VI.

Dimethyl 7-Cyano-8-(1-cyano-1-methoxycarbonylmethyl)-1,9-diazacycl-[3.3.3]azine-2,3-dicarboxylate (15b) Compound **15b** was prepared from **13** in a manner similar to that used for the preparation of **8**. The analytical and spectral data for the product are given in Tables V and VI.

Trimethyl 10,11-Dihydro-9-methyl-11-oxo-6,7,10-triazabenzo[*a*]cycl-[3.3.3]azine-4,5,8-tricarboxylate (16) Compound **16** was prepared from **13** in a manner similar to that used for the preparation of **8**. The analytical and spectral data for the product are given in Tables V and VI.

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