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Studies on Quinolizine Derivatives. XXII.[1] Syntheses and Properties of 2-Phenylazacycl[3.3.3]azine Derivatives

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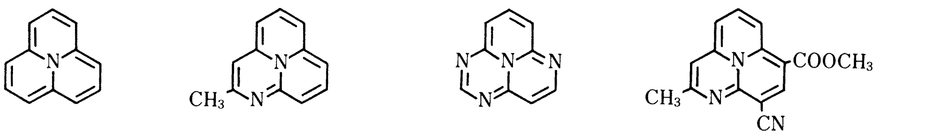
By the reaction of 6-methyl-4-imino-4*H*-quinolizine derivatives (**5**, **8**) with the mixed anhydrides (**6a**—**h**), 2-phenyl-1-azacycl[3.3.3]azines (**7a**—**p**, **9a**—**g**) were obtained. 2-Phenyl-1,3,6-triazacycl[3.3.3]azine derivatives (**15a**—**h**, **17a**—**h**, **18a**—**g**) were prepared by the reaction of 2-(2-cyanovinyl)amino-6-aminopyridines (**13**, **16**) with mixed anhydrides (**6a**—**h**). The proton nuclear magnetic resonance spectral data of the 2-phenylazacycl[3.3.3]azines (**12**, **18a**) may be interpreted in terms of a paramagnetic ring current.

Keywords——2-phenyl-1-azacycl[3.3.3]azine; 2-phenyl-1,3,6-triazacycl[3.3.3]azine; azacyclazine; antiaromatic character; paramagnetic ring current

Since the first synthesis of cycl[3.3.3]azine (**1**) by Farquhar and Leaver,[2] this molecule, which exhibits a paratropic proton nuclear magnetic resonance (^{1}H-NMR) shift, has been examined by Dewar and Trinajstic,[3] who have advanced a simple and convincing argument to show that **1** is aptly characterized as a nitrogen-bridged, "antiaromatic" [12]annulene. Previously, we reported the syntheses of various azacycl[3.3.3]azine derivatives.[4] As part of our continuing studies on azacycl[3.3.3]azines, we now wish to report the synthesis of 2-phenylazacycl[3.3.3]azine derivatives (**7**, **9**, **15**, **17**, **18**), and the effect of the phenyl group on the azacyclazine ring.

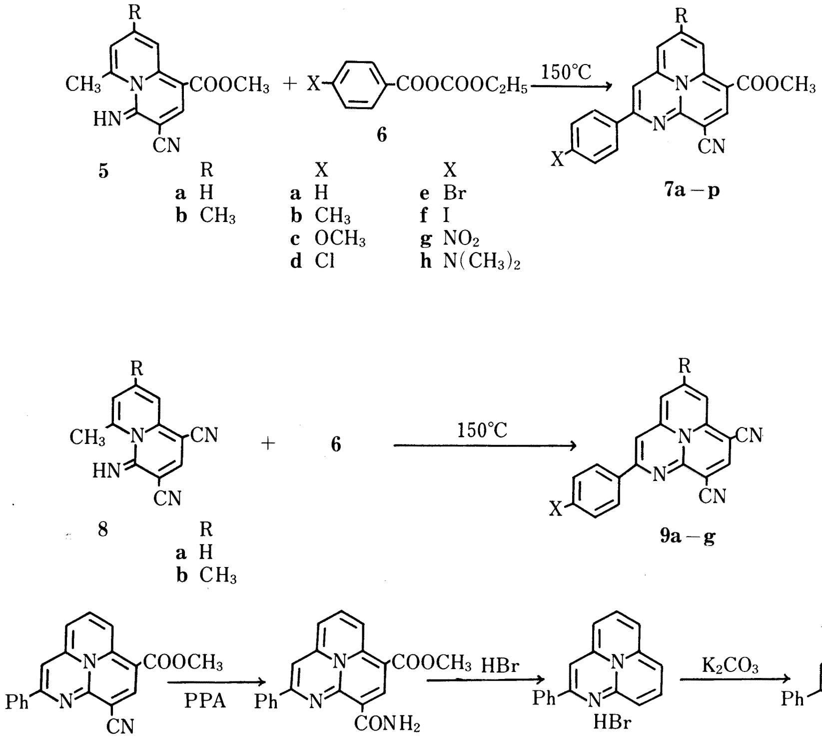


1 **2** **3** **4**

Chart 1

Syntheses of 2-Phenyl-1-azacycl[3.3.3]azines

Previously, we reported a convenient method for the preparation of a 2-methyl-1-azacycl[3.3.3]azine derivative (**4**) by the reaction of 4-imino-6-methyl-4*H*-quinolizine derivative (**5**) with acetic anhydride.[4a] In this paper, we describe an alternative preparation of 2-aryl-1-azacycl[3.3.3]azine derivatives (**7**, **9**) using ethyl *p*-substituted benzoyloxyformates, the mixed anhydrides (**6a**—**h**), which were prepared by the reaction of corresponding *p*-substituted benzoic acids with ethyl chloroformate in the presence of pyridine. Thus, methyl 2-aryl-9-cyano-1-azacycl[3.3.3]azine-7-carboxylates (**7a**—**p**) were obtained by the reaction of **5** and the corresponding mixed anhydrides (**6**) at 150 °C for 3 h in the yields shown in Table I. Compounds **9a**—**g** were also obtained by the reaction of **8** with the mixed anhydrides (**6**) in a similar manner.



5 6 7a−p

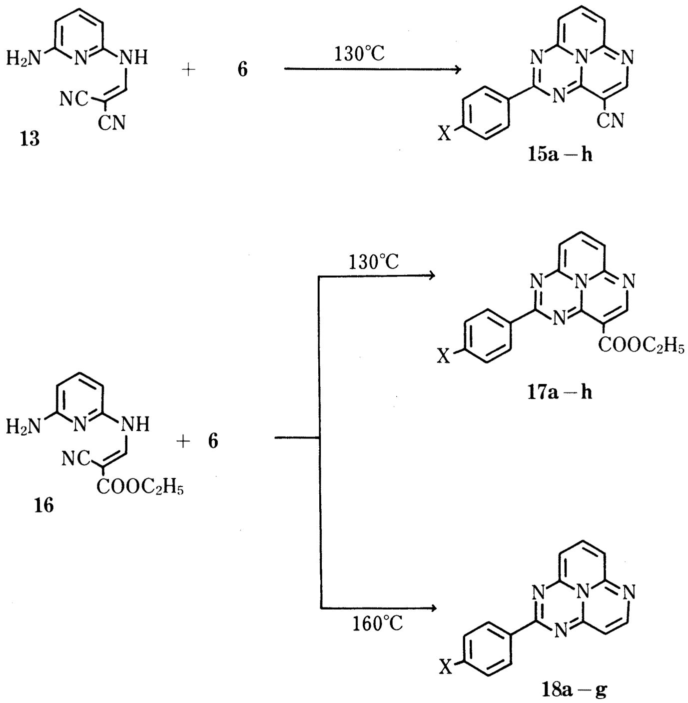
R		X		X
a H		a H		e Br
b CH_3		b CH_3		f I
		c OCH_3		g NO_2
		d Cl		h $N(CH_3)_2$

8 9a−g

R
a H
b CH_3

7a 10 11 12

Chart 2



13 15a−h 16 17a−h 18a−g

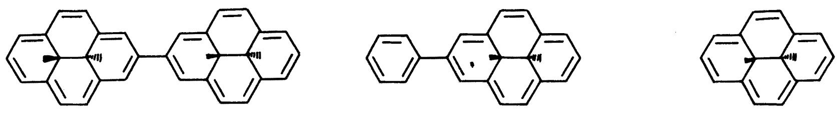
Chart 3

In order to obtain the parent base of **7a**, we examined various conditions for removal of its methoxycarbonyl and cyano groups, and succeeded in the isolation of 2-phenyl-1-azacycl[3.3.3]azine (**12**) as an unstable compound. Thus, a mixture of **7a** and polyphosphoric acid (PPA) was heated at 100 °C for 10 h to give methyl 2-phenyl-9-carbamoyl-1-azacycl[3.3.3]azine-7-carboxylate (**10**) in good yield. Then, a solution of **10** in 47% hydrobromic acid was refluxed for 4 h to give 2-phenyl-1-azacycl[3.3.3]azine hydrobromide (**11**) in good yield. The free base, 2-phenyl-1-azacycl[3.3.3]azine (**12**) was obtained as a greenish brown precipitate by treatment of **11** with potassium carbonate solution but the product was unstable and could not be purified by recrystallization. The ^{1}H-NMR spectrum of the crude free base (**12**) in $CDCl_3$ was recorded as shown in Fig. 1.

The signals for all of the azacyclazine ring protons of **12** appear at δ (ppm): 4.0—6.80, a region in accord with the presence of a paratropic ring current. The result clearly establishes that conjugation between the azacyclazine ring and the benzene ring in **12** reduces the paramagnetic ring current compared with 2-methyl-1-azacycl[3.3.3]azine (**2**),[4a,e] but compound **12** still has antiaromatic character.

Syntheses of 2-Phenyl-1,3,6-triazacycl[3.3.3]azines

Ceder and his co-workers reported the synthesis of 4-cyano-2-methyl-1,3,6-triazacycl[3.3.3]azine (**14**) though a rather troublesome route in 3% yield.[5] We attempted instead to apply the above mixed anhydride method to the synthesis of 2-aryl-1,3,6-triazacycl[3.3.3]azine derivatives. Thus, 2-(2,2-dicyanovinyl)amino-6-aminopyridine (**13**) was reacted with mixed anhydrides (**6a**—**h**) at 130 °C for 3 h to give the corresponding 2-aryl-4-cyano-1,3,6-triazacycl[3.3.3]azines (**15a**—**h**) in good yields. In a similar manner, compounds (**17a**—**h**) were also obtained in good yields of 62—88% by the reaction of 2-(2-cyano-2-ethoxycarbonylvinyl)amino-6-aminopyridine (**16**) with the mixed anhydrides (**6**). When



19 **20** **21**

Chart 4

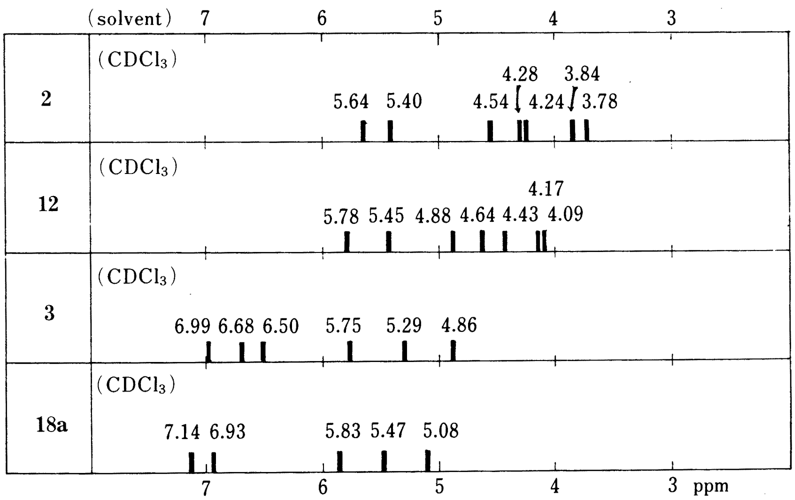


Fig. 1. ^{1}H-NMR Spectral Data for Azacyclazine Derivatives

compound **16** was allowed to react with the mixed anhydrides (**6**) at 160 °C for 3 h, the decarboxylated products, 2-phenyl-1,3,6-triazacycl[3.3.3]azines (**18a**—**g**), were obtained in low yields.

Ceder and his co-workers synthesized 1,3,6-triazacycl[3.3.3]azine (**3**) and found that its proton signals in the ^{1}H-NMR spectrum appeared at relatively low field (δ: 4.8—7.3), which suggested that **3** had aromatic character.[6] The macrocyclic nonbenzenoid biphenyl (**19**) and mixed biphenyl (**20**) have been synthesized in order to examine the effect of the phenyl group on the magnetic current of annulene.[7] Lai reported that a decrease in the ring current is observed in going from the parent 10b,10c-dimethyldihydropyrene (**21**) to **20**, which is consistent with a reduction of delocalization in the macro ring due to increasing conjugation.[8] On the basis of Lai's concepts, the signals of **18a** should be shifted to higher magnetic field than those of **3**, if compound **3** has aromatic character. However, due to increasing conjugation between the 1,3,6-triazacycl[3.3.3]azine ring and the benzene ring in **18a**, the signals are shifted to a lower magnetic field than those of **3** as shown in Fig. 1. Namely, a decrease in the paratropic ring current is observed in going from the parent **4** to **18a**, which is consistent with a reduction in delocalization in the 1,3,6-triazacyclazine ring due to increasing conjugation. We are in the process of preparing other cyclazines with the aim of extending our understanding of these interesting compounds.

Experimental

Melting points were determined with a Mitamura Mel-Temp and are uncorrected. Infrared (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.

General Procedures for Reaction of 5 or 8 with the Mixed Anhydrides (6)——Ethyl chloroformate (0.05 mol) was added dropwise to a stirred mixture of *p*-substituted benzoic acid (0.05 mol) and pyridine (0.05 mol) in $CHCl_3$ over a period of 1 h under ice-cooling. The mixture was stirred overnight at room temperature, and evaporated under reduced pressure. A mixture of the residue (**6**) and **5** or **8** (0.01 mol) was heated at 150 °C for 3 h. The reaction mixture was poured into 300 ml of ice-water. The solution was made basic to litmus with K_2CO_3 and extracted with $CHCl_3$

TABLE I. Analytical Data for **7**

No.	X	R	mp (°C)	Yield (%)	Formula	Analysis (%) Calcd C	H	N	Found C	H	N
7a	H	H	248	20	$C_{20}H_{13}N_3O_2$	73.38	4.00	12.84	73.15	3.96	12.90
7b	CH_3	H	242	15	$C_{21}H_{15}N_3O_2$	73.89	4.43	12.31	74.10	4.36	12.16
7c	CH_3O	H	246	15	$C_{21}H_{15}N_3O_3$	70.58	4.23	11.76	70.42	4.16	11.61
7d	Cl	H	257	20	$C_{20}H_{12}ClN_3O_2$	66.40	3.34	11.61	66.11	3.18	11.37
7e	Br	H	245	15	$C_{20}H_{12}BrN_3O_2$	59.13	2.98	10.34	58.88	2.91	10.16
7f	I	H	248	15	$C_{20}H_{12}IN_3O_2$	53.00	2.67	9.27	52.80	2.54	9.35
7g	NO_2	H	248	20	$C_{20}H_{12}N_4O_4$	64.52	3.25	15.05	64.28	3.30	14.83
7h	$N(CH_3)_2$	H	251	10	$C_{22}H_{18}N_4O_2$	71.34	4.90	15.13	71.17	4.73	15.16
7i	H	CH_3	263	17	$C_{21}H_{15}N_3O_2$	73.89	4.43	12.31	73.60	4.53	12.19
7j	CH_3	CH_3	243	15	$C_{22}H_{17}N_3O_2$	74.35	4.82	11.82	74.55	4.80	11.75
7k	CH_3O	CH_3	183	12	$C_{22}H_{17}N_3O_3$	71.15	4.61	11.31	71.07	4.60	11.11
7l	Cl	CH_3	279	15	$C_{21}H_{14}ClN_3O_2$	67.12	3.76	11.18	67.35	3.65	10.93
7m	Br	CH_3	260	17	$C_{21}H_{14}BrN_3O_2$	60.02	3.36	10.00	59.98	3.26	9.83
7n	I	CH_3	265	10	$C_{21}H_{14}IN_3O_2$	53.98	3.02	8.99	53.72	2.97	8.94
7o	NO_2	CH_3	256	18	$C_{21}H_{14}N_4O_4$	65.28	3.65	14.50	65.41	3.48	14.39
7p	$N(CH_3)_2$	CH_3	258	12	$C_{23}H_{20}N_4O_2$	71.86	5.24	14.57	71.59	5.36	14.80

TABLE II. Spectral Data for **7**

No.	IR (KBr) cm^{-1}	UV λ_{max}^{EtOH} nm ($\log \varepsilon$)	^{1}H-NMR δ (ppm) C_3-H	C_4-H, C_6-H	C_5-H	C_8-H	Others
7a	1690 (C=O) 2200 (CN)	276,[a] 312 sh, 325, 408, 424, 448	5.58 (s)	5.45, 7.23 (dd) (dd)	6.54 (t)	7.09 (s)	3.63 (3H, s, OCH_3),[b] 7.31—7.74 (5H, m, Ar-H)
7b	1690 (C=O) 2200 (CN)	274 (4.31), 332 (4.64), 406 (4.37), 423 (4.40), 447 (4.52)	5.58 (s)	5.47, 7.13 (dd) (dd)	6.52 (t)	7.08 (s)	2.26 (3H, s, CH_3),[b] 3.63 (3H, s, OCH_3), 7.13 (2H, d, J=8 Hz, Ar-H), 7.50 (2H, d, J=8 Hz, Ar-H)
7c	1695 (C=O) 2200 (CN)	270 (4.36), 310 (4.15) sh, 350 (4.66), 404 (4.39), 424 (4.44), 446 (4.57)	5.56 (s)	5.48, 7.20 (dd) (dd)	6.51 (t)	7.07 (s)	3.62 (3H, s, OCH_3),[b] 3.88 (3H, s, OCH_3), 6.86 (2H, d, J=9 Hz, Ar-H), 7.61 (2H, d, J=9 Hz, Ar-H)
7d	1700 (C=O) 2200 (CN)	276,[a] 318 sh, 330, 412, 424, 450	5.53 (s)	5.46, 7.25 (dd) (dd)	6.54 (t)	7.09 (s)	3.64 (3H, s, OCH_3),[b] 7.30 (2H, d, J=8 Hz, Ar-H), 7.62 (2H, d, J=8 Hz, Ar-H)
7e	1695 (C=O) 2200 (CN)	277,[a] 320 sh, 331, 412, 425, 451	5.53 (s)	5.47, 7.26 (dd) (dd)	6.54 (t)	7.08 (s)	3.64 (3H, s, OCH_3),[b] 7.31 (4H, s, Ar-H)
7f	1695 (C=O) 2200 (CN)	275,[a] 335, 417, 426, 452	5.54 (s)	5.46, 7.26 (dd) (dd)	6.54 (t)	7.09 (s)	3.64 (3H, s, OCH_3),[b] 7.38 (2H, d, J=8 Hz, Ar-H), 7.69 (2H, d, J=8 Hz, Ar-H)
7g	1690 (C=O) 2200 (CN)	282 sh,[a] 326, 370 sh, 424, 448	5.57 (s)	5.47, 7.31 (dd) (dd)	6.56 (t)	7.09 (s)	3.64 (3H, s, OCH_3),[b] 7.79 (2H, d, J=9 Hz, Ar-H), 8.18 (2H, d, J=9 Hz, Ar-H)
7h	1680 (C=O) 2200 (CN)	272,[a] 313 sh, 400, 412, 453	5.55 (s)	5.48, 7.22 (dd) (dd)	6.49 (t)	7.10 (s)	3.00 (6H, s, $NCH_3 \times 2$),[b] 3.63 (3H, s, OCH_3), 6.68 (2H, d, J=9 Hz, Ar-H), 7.66 (2H, d, J=9 Hz, Ar-H)
7i	1680 (C=O) 2200 (CN)	276,[a] 310 sh, 324, 405 sh, 418, 442	5.64 (s)	5.45, 7.39 (s) (s)		7.18 (s)	1.87 (3H, s, CH_3),[b] 3.64 (3H, s, OCH_3), 7.45—7.76 (5H, m, Ar-H)
7j	1680 (C=O) 2200 (CN)	270,[a] 332, 404, 420, 444	5.63 (s)	5.42, 7.41 (s) (s)		7.14 (s)	1.85 (3H, s, CH_3),[b] 2.35 (3H, s, CH_3), 3.63 (3H, s, OCH_3), 7.09—7.71 (4H, m, Ar-H)
7k	1680 (C=O) 2200 (CN)	270 (4.32), 348 (4.60), 404 (4.36), 420 (4.38), 444 (4.47)	5.60 (s)	5.46, 7.21 (s) (s)		7.18 (s)	1.87 (3H, s, CH_3),[b] 3.64 (3H, s, OCH_3), 3.82 (3H, s, OCH_3), 6.84 (2H, d, J=9 Hz, Ar-H), 7.68 (2H, d, J=9 Hz, Ar-H)
7l	1690 (C=O) 2200 (CN)	250 (4.13) sh, 276 (4.33), 316 (4.61) sh, 327 (4.66), 410 (4.41) sh, 418 (4.44), 442 (4.50)	6.27 (s)	5.82, 7.14 (s) (s)		7.10 (s)	1.88 (3H, s, CH_3),[c] 3.57 (3H, s, OCH_3), 7.48 (2H, d, J=9 Hz, Ar-H), 7.72 (2H, d, J=9 Hz, Ar-H)
7m	1680 (C=O) 2200 (CN)	250 sh,[a] 276, 318 sh, 336, 410 sh, 418, 443	6.27 (s)	5.82, 7.13 (s) (s)		7.10 (s)	1.88 (3H, s, CH_3),[c] 3.57 (3H, s, OCH_3), 7.64 (4H, s, Ar-H)
7n	1690 (C=O) 2200 (CN)	275,[a] 320 sh, 338, 396 sh, 420, 444	5.60 (s)	5.43, 7.22 (s) (s)		7.17 (s)	1.87 (3H, s, CH_3),[b] 3.65 (3H, s, OCH_3), 7.40 (2H, d, J=9 Hz, Ar-H), 7.71 (2H, d, J=9 Hz, Ar-H)
7o	1700 (C=O) 2200 (CN)	280 sh,[a] 332, 420, 444	5.62 (s)	5.43, 7.28 (s) (s)		7.17 (s)	1.89 (3H, s, CH_3),[b] 3.66 (3H, s, OCH_3), 7.70 (2H, d, J=9 Hz, Ar-H), 8.18 (2H, d, J=9 Hz, Ar-H)
7p	1690 (C=O) 2200 (CN)	260,[a] 312 sh, 400, 426, 448	5.58 (s)	5.44, 7.35 (s) (s)		7.15 (s)	1.85 (3H, s, CH_3),[b] 3.01 (6H, s, $NCH_3 \times 2$), 3.64 (3H, s, OCH_3), 6.61 (2H, d, J=9 Hz, Ar-H), 7.65 (2H, d, J=9 Hz, Ar-H)

a) Concentration is unknown because of poor solubility. *b*) The solvent used was $CDCl_3$. *c*) The solvent used was DMSO-d_6.
s = singlet, dd = double doublet (J=8, 1 Hz), t = triplet (J=8 Hz).

(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–$CHCl_3$ (1 : 1) fraction, the corresponding 2-phenyl-1-azacycl[3.3.3]azine derivatives (**7** or **9**) were obtained. The analytical and spectral data for the products are given in Tables I—IV.

TABLE III. Analytical Data for **9**

No.	X	R	mp (°C)	Yield (%)	Formula	Analysis (%) Calcd C	H	N	Found C	H	N
9a	H	H	>300	22	$C_{19}H_{10}N_4$	77.54	3.43	19.04	77.43	3.38	18.78
9b	CH_3	H	>300	20	$C_{20}H_{12}N_4$	77.91	3.92	18.17	77.78	3.85	18.10
9c	Cl	H	>300	16	$C_{19}H_9ClN_4$	69.41	2.76	17.04	69.43	2.80	17.32
9d	Br	H	>300	18	$C_{19}H_9BrN_4$	61.15	2.43	15.01	61.31	2.58	14.75
9e	H	CH_3	>300	14	$C_{20}H_{12}N_4$	77.91	3.91	18.17	77.97	3.67	17.95
9f	CH_3	CH_3	>300	10	$C_{21}H_{14}N_4$	78.24	4.38	17.38	78.36	4.30	17.15
9g	CH_3O	CH_3	>300	16	$C_{21}H_{14}N_4O$	74.54	4.17	16.56	74.82	4.27	16.29

TABLE IV. Spectral Data for **9**

No.	IR (KBr) cm^{-1}	UV λ_{max}^{EtOH} nm ($\log \varepsilon$)	^{1}H-NMR δ (ppm) C_3-H	C_4-H, C_6-H	C_5-H	C_8-H	Others
9a	2200 (CN)	276,[a] 329, 400 sh, 410 sh, 418, 440	6.19 (s)	5.67, 5.76 (dd) (dd)	6.77 (t)	6.87 (s)	7.39—7.88 (5H, m, Ar-H)[b]
9b	2200 (CN)	273,[a] 336, 396 sh, 410 sh, 418, 440	6.17 (s)	5.66, 5.73 (dd) (dd)	6.76 (t)	6.89 (s)	2.33 (3H, s, CH_3),[b] 7.23 (2H, d, J=8 Hz, Ar-H), 7.59 (2H, d, J=8 Hz, Ar-H)
9c	2200 (CN)	274,[a] 330, 398 sh, 410 sh, 418, 442	6.23 (s)	5.72, 5.75 (dd) (dd)	6.80 (t)	6.95 (s)	7.50 (2H, d, J=8 Hz, Ar-H),[b] 7.70 (2H, d, J=8 Hz, Ar-H)
9d	2200 (CN)	274,[a] 332, 398 sh, 410 sh, 419, 441	6.22 (s)	5.71, 5.74 (dd) (dd)	6.79 (t)	6.91 (s)	7.62 (4H, s, Ar-H)[b]
9e	2200 (CN)	248 sh,[a] 274, 334, 388 sh, 412, 436	6.21 (s)	5.65, 5.72 (s) (s)		6.95 (s)	1.85 (3H, s, CH_3),[b] 7.39—7.76 (5H, m, Ar-H)
9f	2200 (CN)	246 sh,[a] 273, 325, 390 sh, 412, 436	6.18 (s)	5.61, 5.70 (s) (s)		6.95 (s)	1.84 (3H, s, CH_3),[b] 2.33 (3H, s, CH_3), 7.23 (2H, d, J=8 Hz, Ar-H), 7.61 (2H, d, J=8 Hz, Ar-H)
9g	2200 (CN)	274,[a] 302 sh, 354, 415, 458	6.14 (s)	5.57, 5.69 (s) (s)		6.93 (s)	1.84 (3H, s, CH_3),[b] 3.79 (3H, s, OCH_3), 6.96 (2H, d, J=9 Hz, Ar-H), 7.67 (2H, d, J=9 Hz, Ar-H)

a) Concentration is unknown because of poor solubility. *b*) The solvent used was DMSO-d_6. s = singlet, dd = double doublet (J=8, 1 Hz), t = triplet (J=8 Hz).

TABLE V. Analytical Data for **15**

No.	X	mp (°C)	Yield (%)	Formula	Analysis (%) Calcd C	H	N	Found C	H	N
15a	H	138	95	$C_{16}H_9N_5$	70.84	3.34	25.82	70.97	3.28	25.55
15b	CH_3	179	84	$C_{17}H_{11}N_5$	71.57	3.89	24.55	71.51	3.81	24.47
15c	CH_3O	288	86	$C_{17}H_{11}N_5O$	67.77	3.68	23.24	67.71	3.71	23.13
15d	Cl	280	72	$C_{16}H_8ClN_5$	62.86	2.64	22.91	62.62	2.54	22.91
15e	Br	278	90	$C_{16}H_8BrN_5$	54.88	2.30	20.00	54.66	2.22	19.90
15f	I	312	70	$C_{16}H_8IN_5$	48.39	2.03	17.63	48.52	2.31	17.84
15g	NO_2	280	94	$C_{16}H_8N_6O_2$	60.76	2.55	26.57	60.72	2.45	26.30
15h	$N(CH_3)_2$	273	77	$C_{18}H_{14}N_6$	68.78	4.49	26.73	68.62	4.39	26.58

TABLE VI. Spectral Data for **15**

No.	IR (KBr) cm^{-1}	UV λ_{max}^{EtOH} nm ($\log \varepsilon$)	^{1}H-NMR δ (ppm) C_5-H	C_7-H, C_9-H	C_8-H	Others
15a	2200 (CN)	234 (4.36) sh, 260 (4.08) sh, 310 (4.61), 345 (4.23), 350 (4.22) sh, 369 (4.12), 377 (4.24), 396 (4.23)	7.37 (s)	6.03, 6.13 (dd) (dd)	7.16 (t)	7.40—7.55 (3H, m, Ar-H),[b)] 8.06—8.16 (2H, m, Ar-H)
15b	2200 (CN)	222 sh,[a)] 230 sh, 244, 270 sh, 325, 362 sh, 379, 398 sh	7.57 (s)	6.07, 6.18 (dd) (dd)	7.35 (t)	2.38 (3H, s, CH_3),[c)] 7.28 (2H, d, $J=9$ Hz, Ar-H), 7.89 (2H, d, $J=9$ Hz, Ar-H)
15c	2200 (CN)	228 (4.39), 252 (4.26) sh, 262 (4.14) sh, 272 (4.04) sh, 288 (3.94) sh, 346 (4.79), 352 (4.76) sh, 378 (4.41), 398 (4.26)	7.28 (s)	6.12, 6.34 (dd) (dd)	7.28 (t)	3.87 (3H, s, OCH_3),[b)] 6.92 (2H, d, $J=9$ Hz, Ar-H), 7.90 (2H, d, $J=9$ Hz, Ar-H)
15d	2200 (CN)	220 sh,[a)] 240, 263 sh, 315, 347, 360 sh, 379, 397	7.60 (s)	6.09, 6.21 (dd) (dd)	7.37 (t)	7.54 (2H, d, $J=9$ Hz, Ar-H),[c)] 7.77 (2H, d, $J=9$ Hz, Ar-H)
15e	2200 (CN)	220 sh,[a)] 241, 264 sh, 317, 350 sh, 360 sh, 378, 397	7.59 (s)	6.08, 6.21 (dd) (dd)	7.36 (t)	7.63—7.94 (4H, m, Ar-H)[c)]
15f	2200 (CN)	220 sh,[a)] 243, 256 sh, 328, 352 sh, 362 sh, 380, 392 sh, 400	7.37 (s)	6.00, 6.13 (dd) (dd)	7.16 (t)	7.74—7.88 (4H, m, Ar-H)[b)]
15g	2200 (CN)	244 sh,[a)] 305, 323 sh, 363, 382, 401	7.61 (s)	6.12, 6.25 (dd) (dd)	7.39 (t)	8.14 (2H, d, $J=9$ Hz, Ar-H),[c)] 8.32 (2H, d, $J=9$ Hz, Ar-H)
15h	2200 (CN)	218 (4.54) sh, 230 (4.48) sh, 240 (4.44) sh, 273 (4.23), 280 (4.15) sh, 350 (4.52), 352 (4.38), 404 (4.56) sh, 429 (4.68)	7.37 (s)	5.99, 6.05 (dd) (dd)	7.11 (t)	3.07 (6H, s, $NCH_3 \times 2$),[b)] 6.51 (2H, d, $J=9$ Hz, Ar-H), 8.05 (2H, d, $J=9$ Hz, Ar-H)

a) Concentration is unknown because of poor solubility. *b)* The solvent used was $CDCl_3$. *c)* The solvent used was DMSO-d_6. s = singlet, dd = double doublet ($J=8$, 1 Hz), t = triplet ($J=8$ Hz).

TABLE VII. Analytical Data for **17**

No.	X	mp (°C)	Yield (%)	Formula	Analysis (%) Calcd C	H	N	Found C	H	N
17a	H	170	80	$C_{18}H_{14}N_4O_2$	67.93	4.43	17.60	68.12	4.28	17.51
17b	CH_3	182	75	$C_{19}H_{16}N_4O_2$	68.66	4.85	16.86	68.47	4.83	16.58
17c	CH_3O	198	73	$C_{19}H_{16}N_4O_3$	65.51	4.63	16.08	65.72	4.49	16.04
17d	Cl	228	73	$C_{18}H_{13}ClN_4O_2$	61.28	3.72	15.88	61.44	3.63	15.70
17e	Br	238	88	$C_{18}H_{13}BrN_4O_2$	54.43	3.30	14.10	54.19	3.13	13.84
17f	I	248	83	$C_{18}H_{13}IN_4O_2$	48.67	2.95	12.61	48.61	2.91	12.60
17g	NO_2	285	62	$C_{18}H_{13}N_5O_4$	59.51	3.61	19.28	59.46	3.55	18.99
17h	$N(CH_3)_2$	187	66	$C_{20}H_{19}N_5O_2$	66.47	5.30	19.38	66.30	5.24	19.53

Methyl 9-Carbamoyl-2-phenyl-1-azacycl[3.3.3]azine-7-carboxylate (10)——A mixture of **7a** (0.5 g) and an excess of PPA (10 g) was heated at 100 °C for 10 h. The reaction mixture was poured into ice-water (300 ml). The solution was made basic to litmus with K_2CO_3, and extracted with $CHCl_3$ (3 × 50 ml). The extract was washed with water (50 ml), dried (Na_2SO_4), and evaporated under reduced pressure to give crude crystals **10** (95%), which were recrystallized from $CHCl_3$–MeOH as green needles, mp > 300 °C. *Anal.* Calcd for $C_{20}H_{15}N_3O_3$: C, 69.56; H, 4.38; N, 12.17. Found: C, 69.56; H, 4.57; N, 12.07. IR (KBr) cm^{-1}: 1670 (C=O), 1620 (C=O), 3300 (NH). UV λ_{max}^{EtOH} nm: 275, 309, 407, 422, 446. ^{1}H-NMR ($CDCl_3$–F_3CCOOH) δ (ppm): 3.84 (3H, s, OCH_3), 5.84 (1H, s, C_3-H), 6.44 (1H, dd, $J=8$, 1 Hz, C_4-H or C_6-H), 7.36—7.64 (6H, m, C_5-H and Ar-H), 8.10 (1H, s, C_8-H), 8.14 (1H, dd, $J=8$, 1 Hz, C_4-H or C_6-H).

2-Phenyl-1-azacycl[3.3.3]azine Hydrobromide (11)——A solution of **10** (0.5 g) in 47% HBr (20 ml) was refluxed for 3 h. The solution was evaporated under reduced pressure. The residue was recrystallized from MeOH to give **11** in

TABLE VIII. Spectral Data for **17**

No.	IR (KBr) cm^{-1}	UV λ_{max}^{EtOH} nm (log ε)	^{1}H-NMR δ (ppm) C_5-H	C_7-H, C_9-H	C_8-H	Others
17a	1680 (C=O)	224 (4.18) sh, 238 (4.32), 246 (4.26) sh, 262 (4.10) sh, 309 (4.62), 348 (4.30), 366 (4.13), 383 (4.28), 400 (4.26)	7.88 (s)	5.95, 6.10 (dd) (dd)	7.08 (t)	1.36 (3H, t, J=7 Hz, $OCH_2\underline{CH_3}$),[b] 4.25 (2H, q, J=7 Hz, $O\underline{CH_2}CH_3$), 7.27—7.52 (3H, m, Ar-H), 8.07—8.17 (2H, m, Ar-H)
17b	1670 (C=O)	241 (4.36), 272 (4.05) sh, 321 (4.66), 345 (4.36) sh, 366 (4.36), 384 (4.27), 401 (4.26)	7.88 (s)	5.93, 6.07 (dd) (dd)	7.07 (t)	1.35 (3H, t, J=7 Hz, $OCH_2\underline{CH_3}$),[b] 2.39 (3H, s, CH_3), 4.25 (2H, q, J=7 Hz, $O\underline{CH_2}CH_3$), 7.13—7.24 (2H, m, Ar-H), 7.90—8.06 (2H, m, Ar-H)
17c	1710 (C=O)	241,[a] 266, 345, 380, 400	7.90 (s)	5.93, 6.09 (dd) (dd)	7.08 (t)	1.36 (3H, t, J=7 Hz, $OCH_2\underline{CH_3}$),[b] 3.85 (3H, s, OCH_3), 4.26 (2H, q, J=7 Hz, $O\underline{CH_2}CH_3$), 6.87 (2H, d, J=9 Hz, Ar-H), 8.11 (2H, d, J=9 Hz, Ar-H)
17d	1680 (C=O)	224 sh,[a] 238, 312, 349, 366, 382, 400	7.87 (s)	5.90, 6.11 (dd) (dd)	7.07 (t)	1.34 (3H, t, J=7 Hz, $OCH_2\underline{CH_3}$),[b] 4.24 (2H, q, J=7 Hz, $O\underline{CH_2}CH_3$), 7.33 (2H, d, J=9 Hz, Ar-H), 8.05 (2H, d, J=9 Hz, Ar-H)
17e	1680 (C=O)	234 sh,[a] 262 sh, 313, 348, 364, 380, 399	7.89 (s)	5.92, 6.13 (dd) (dd)	7.10 (t)	1.35 (3H, t, J=7 Hz, $OCH_2\underline{CH_3}$),[b] 4.25 (2H, q, J=7 Hz, $O\underline{CH_2}CH_3$), 7.34 (2H, d, J=9 Hz, Ar-H), 8.05 (2H, d, J=9 Hz, Ar-H)
17f	1680 (C=O)	224 sh,[a] 244, 326, 350 sh, 386, 404	7.87 (s)	5.91, 6.10 (dd) (dd)	7.07 (t)	1.34 (3H, t, J=7 Hz, $OCH_2\underline{CH_3}$),[b] 4.24 (2H, q, J=7 Hz, $O\underline{CH_2}CH_3$), 7.66—7.87 (4H, m, Ar-H)
17g	1710 (C=O)	247,[a] 307, 322, 364, 390, 408	7.86 (s)	5.92, 6.14 (dd) (dd)	7.09 (t)	1.35 (3H, t, J=7 Hz, $OCH_2\underline{CH_3}$),[b] 4.26 (2H, q, J=7 Hz, $O\underline{CH_2}CH_3$), 8.22 (4H, s, Ar-H)
17h	1670 (C=O)	220 (4.44) sh, 244 (4.39), 268 (4.17), 348 (4.47), 366 (4.32) sh, 384 (4.44) sh, 408 (4.63) sh, 422 (4.64)	7.91 (s)	5.92, 6.05 (dd) (dd)	7.06 (t)	1.37 (3H, t, J=7 Hz, $OCH_2\underline{CH_3}$),[b] 3.05 (6H, s, $NCH_3 \times 2$), 4.24 (2H, q, J=7 Hz, $O\underline{CH_2}CH_3$), 6.64 (2H, d, J=9 Hz, Ar-H), 8.04 (2H, d, J=9 Hz, Ar-H)

a) Concentration is unknown because of poor solubility. *b*) The solvent used was $CDCl_3$. s=singlet, dd=double doublet (J=8, 1 Hz), t=triplet (J=8 Hz).

TABLE IX. Analytical Data for **18**

No.	X	mp (°C)	Yield (%)	Formula	Analysis (%) Calcd C	H	N	Found C	H	N
18a	H	163	19	$C_{15}H_{10}N_4$	73.16	4.09	22.75	72.93	4.04	22.69
18b	CH_3	235	16	$C_{16}H_{12}N_4$	73.83	4.65	21.52	74.08	4.64	21.51
18c	CH_3O	187	23	$C_{16}H_{12}N_4O$	69.55	4.38	20.28	69.45	4.40	20.03
18d	Cl	274	24	$C_{15}H_9ClN_4$	64.18	3.23	19.96	64.05	3.08	20.04
18e	Br	260	21	$C_{15}H_9BrN_4$	55.41	2.79	17.23	55.21	2.71	17.10
18f	I	265	18	$C_{15}H_9IN_4$	48.41	2.44	15.05	48.34	2.35	15.30
18g	NO_2	249	18	$C_{15}H_9N_5O_2$	61.86	3.11	24.04	61.60	3.00	23.89

TABLE X. Spectral Data for **18**

No.	UV λ_{max}^{EtOH} nm ($\log\varepsilon$)	^{1}H-NMR δ (ppm) C_4-H	C_5-H	C_7-H, C_9-H	C_8-H	Others
18a	234 (4.28), 304 (4.61), 344 (4.15), 356 (4.18), 362 (4.17) sh, 372 (4.17), 384 (4.06), 392 (4.14)	5.08 (d)	7.14 (d)	5.47, 5.83 (dd) (dd)	6.93 (t)	7.27—7.53 (3H, m, Ar-H),[a] 7.78—7.89 (2H, m, Ar-H)
18b	243 (4.31), 314 (4.66), 356 (4.23), 374 (4.21), 392 (4.18)	4.98 (d)	6.99 (d)	5.40, 5.71 (dd) (dd)	6.68 (t)	2.30 (3H, s, CH_3),[a] 7.07 (2H, d, $J=8$ Hz, Ar-H), 7.74 (2H, d, $J=8$ Hz, Ar-H)
18c	246 (4.32), 339 (4.70), 372 (4.24), 392 (4.16)	5.06 (d)	7.07 (d)	5.48, 5.79 (dd) (dd)	6.76 (t)	3.83 (3H, s, OCH_3),[a] 6.83 (2H, d, $J=9$ Hz, Ar-H), 7.90 (2H, d, $J=9$ Hz, Ar-H)
18d	240 (4.31), 309 (4.70), 346 (4.20), 362 (4.25), 373 (4.24), 392 (4.18)	5.05 (d)	7.08 (d)	5.50, 5.84 (dd) (dd)	6.79 (t)	7.30 (2H, d, $J=9$ Hz, Ar-H),[a] 7.85 (2H, d, $J=9$ Hz, Ar-H)
18e	241 (4.30), 310 (4.67), 346 (4.18), 364 (4.23), 374 (4.22), 392 (4.16)	5.07 (d)	7.07 (d)	5.47, 5.81 (dd) (dd)	6.77 (t)	7.46 (2H, d, $J=9$ Hz, Ar-H),[a] 7.78 (2H, d, $J=9$ Hz, Ar-H)
18f	243 (4.37), 316 (4.72), 364 (4.30), 372 (4.28), 392 (4.24)	5.02 (d)	7.05 (d)	5.44, 5.79 (dd) (dd)	6.75 (t)	7.64 (4H, s, Ar-H)[a]
18g	233 (4.34), 278 (4.37), 333 (4.10), 370 (4.20), 388 (4.12)	4.94 (d)	7.06 (d)	5.37, 5.83 (dd) (dd)	6.75 (t)	7.40—7.75 (4H, m, Ar-H)[a]

a) The solvent used was $CDCl_3$. s = singlet, d = doublet ($J=6$ Hz), dd = double doublet ($J=8$, 1 Hz), t = triplet ($J=8$ Hz).

quantitative yield: mp >300 °C. *Anal.* Calcd for $C_{17}H_{13}BrN_2$: C, 62.79; H, 4.03; N, 8.61. Found: C, 62.66; H, 4.12; N, 8.57. UV λ_{max}^{EtOH} nm ($\log\varepsilon$): 244 (4.06), 254 (4.07), 302 (4.46), 400 (4.11) sh, 408 (4.12), 420 (4.12), 430 (4.16). ^{1}H-NMR (DMSO-d_6) δ (ppm): 5.35 (1H, s, C_3-H), 5.86 (1H, dd, $J=8$, 1 Hz, C_7-H or C_9-H), 5.92 (1H, dd, $J=8$, 1 Hz, C_4-H or C_6-H), 6.31 (1H, dd, $J=8$, 1 Hz, C_7-H or C_9-H), 6.42 (1H, dd, $J=8$, 1 Hz, C_4-H or C_6-H), 6.80 (1H, t, $J=8$ Hz, C_5-H), 7.09 (1H, t, $J=8$ Hz, C_8-H), 7.47 (5H, s, Ar-H).

2-Phenyl-1-azacycl[3.3.3]azine (12)——A solution of **11** (0.5 g) in water (50 ml) was made basic to litmus with K_2CO_3 and immediately extracted with $CHCl_3$ (30 ml). The extract was dried (Na_2SO_4) and evaporated under reduced pressure. The residue was dried in a vacuum desiccator (2 mmHg) for 5 min. The ^{1}H-NMR spectrum of the crude free base **12** was recorded: ^{1}H-NMR ($CDCl_3$) δ (ppm): 4.09 (1H, dd, $J=8$, 1 Hz, C_4-H or C_6-H), 4.17 (1H, s, C_3-H), 4.43 (1H, dd, $J=8$, 1 Hz, C_7-H or C_9-H), 4.64 (1H, dd, $J=8$, 1 Hz, C_7-H or C_9-H), 4.88 (1H, dd, $J=8$, 1 Hz, C_4-H or C_6-H), 5.45 (1H, t, $J=8$ Hz, C_5-H), 5.78 (1H, t, $J=8$ Hz, C_8-H), 7.26 (5H, br s, Ar-H).

General Procedure for the Preparation of 2-Phenyl-1,3,6-triazacycl[3.3.3]azine Derivatives (15, 17)——These compounds (**15**, **17**) were prepared at 130 °C for 3 h from **13** or **16** in a manner similar to that used for the preparation of **7** or **9**. The analytical and spectral data for the products are given in Tables V—VIII.

General Procedure for the Preparation of 2-Phenyl-1,3,6-triazacycl[3.3.3]azines (18)——These compounds (**18**) were prepared at 160 °C for 3 h from **16** in a manner similar to that used for the preparation of **7** or **9**. The analytical and spectral data for the products are given in Tables IX and X.

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