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Model Studies Related to Synthesis and 1,4-Dipolar Cycloaddition Reactions of Mesoionic Heterocycles

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The reaction of 2-(substituted amino)pyridine with reactive malonic acid derivatives provided an extremely facile synthesis of the mesoionic compound 4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-1-ium-2-olates. *N*,*N*′-Disubstituted amidine reacted with diethyl malonate to afford 4-quinolone in a one-pot cyclization and rearrangement (type A/I) of 4-oxo-pyridiniumolate **6**. The latter compound was isolated via a reaction of acyclic amidine with AME's. A cycloaddition reaction of the mesoionic pyrimidine **6** with maleic anhydride or *N*-phenylmaleimide yielded [2+4] cycloadducts. Triphenyl pyrrolopyridinetrione **12** was achieved via a ring transformation of the cycloadduct 4-benzyl-3,5-dioxo-1,2,6-triphenyl-2,6-diazabicyclo[2.2.2]octane-7,8-dicarboxylic anhydride **11d**. In contrast, the cycloadduct 4-ethyl derivative **11c** and substituted 3,5-dioxo-1,2,6-triphenyl-2,6-diazabicyclo[2.2.2]octane-7,8-dicarboxylic *N*-phenylimides did not give **12** under the same reaction conditions. The mechanistic pathway for the formation of **12** was studied. Dimethyl acetylenedicarboxylate reacted with **6b,c** to furnish 2-oxo-1,2-dihydropyridine-4,5-dicarboxylates.

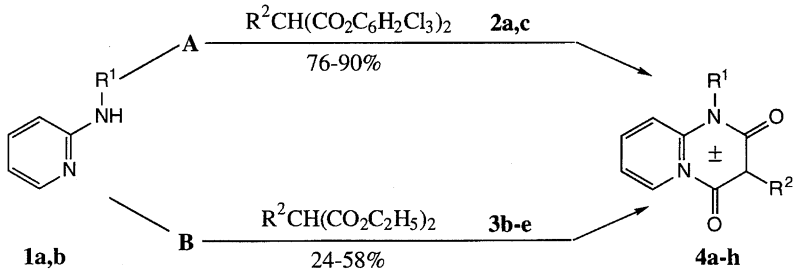
Five- and six-membered heterocyclic mesoionic compounds are well-known.[1—6] These compounds have been shown to be good synthons for the synthesis of various fused heterocyclic systems.[6—13] Mesoions have remained a challenge for crystallographers and theoreticians in exploring the sometimes peculiar bond and electronic properties of these compounds. In recent years, much attention has been focused on the biological and pharmacological activities[14] of the bicyclic six-membered mesoions, which were still unexplored. Mesoionic heterocycles have wide industrial applications e.g. as a nonaqueous electrolyte battery[15] and pressure transfer photothermographic copying materials;[16] some show even marked hair-growth stimulation.[17]

Mesoionic six-membered heterocyclic pyrimidines are regarded as being good precursors for 1,4-dipolar systems with electron-poor or electron-rich multiple bond systems; this promoted us to design a specific program aimed at constructing new *hitherto* unreported heterocyclic pyrimidine systems of expected bioresponses, which are capable of undergoing dipolar [4+2] cycloaddition reactions. The newly synthesized compounds possess latent functional substituents and appear to be promising for further building blocks for a variety of heterocyclic pyrimidine as well as biological-activity evaluations.

Results and Discussion

Bicyclic 4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-1-ium-2-olates **4a—d** were obtained in good yield via the condensation of 2-(substituted amino)pyridine **1a,b** with appropriate bis-(2,4,6-trichlorophenyl)malonates (AME's) **2a,c** (Scheme 1, method A). The reaction was performed without a solvent, not according to the literature methods, which recommend the use of bromobenzene or anisole.[18]

Since 2-aminopyridine can be regarded as an amidine sys-



R¹ **a**: CH_3
b: $CH_2C_6H_5$

R² **a**: C_2H_5
b: C_6H_5
c: $(CH_2)_3CH_3$
d: CH_2-CH=CH_2
e: $(CH_2)_2CN$

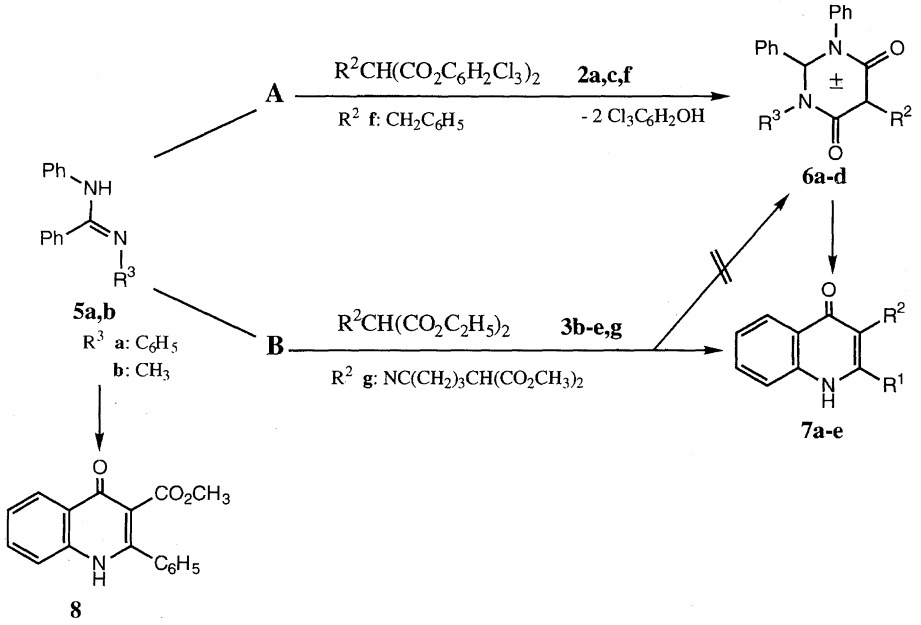
Scheme 1.

tem we extended this general synthetic approach to acyclic amidines to obtain monocyclic six-membered mesoions **6a—d**. Thus, *N*,*N*′-disubstituted amidines **5a**,**b** reacted with AME's **2a**,**c**,**f** via a previously reported pathway[19,20] to yield **6a—d**. One possible explanation for the formation **6a—d** includes ring closure by the loss of 2 molecules of trichlorophenol through a ketene intermediate (Scheme 2, method A). The elemental and spectroscopic data of **4a—d** and **6a—d** are compatible with the assigned structure.

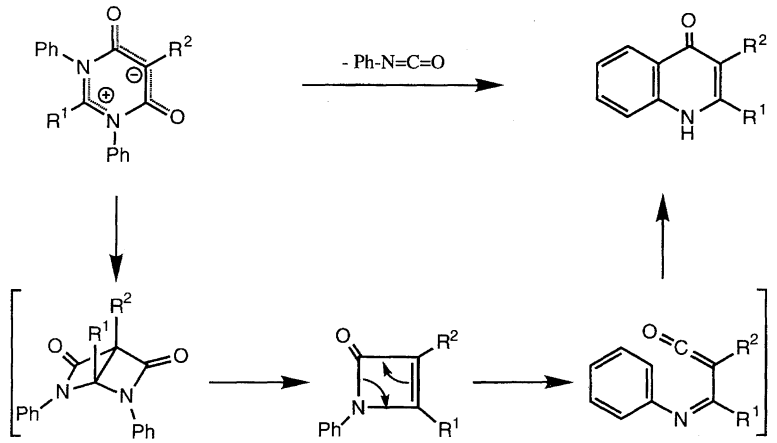
It has been reported that an elevated temperature and a longer reaction time should be avoided, since the liberated trichlorophenol would catalyze the conversion of the mesoion of type **6** into 4-quinolones of type **7**.[20] Surprisingly, when diethyl malonates **3** were refluxed with *N*,*N*′-diphenylbenzamidine **5a** in tetralin as a solvent, it furnished rearranged 4-quinolones **7a—e** directly without the isolation of compound **6**, (Scheme 2, method B). The mechanism of this rearrangement can be rationalized by the formation of compound **6** via condensation of **5** with the malonate **3**. Bond formation between C-2 and C-5 (simultaneous), and the loss of phenyl isocyanate with substituent ring opening to the valence tautomeric ketene took place; then, ring closure occurred to afford the 4-quinolone **7** via a type A/I rearrangement[20] (Scheme 3). The elemental analysis and spectroscopic data are in agreement with the proposed structure **7**. The IR spectrum of **7a**, as a representative example, displayed an NH at ν_{max} 3030 cm^{-1}, C=O at ν_{max} 1548, and 1503 cm^{-1}, where ^1H NMR spectrum revealed δ = 0.72 (t, 3H, CH_3, J = 7 Hz), 1.08—1.48 (m, 4H, CH_2CH_2), 2.39 (t, 2H, CH_2, J = 7 Hz), 7.22—7.68 (m, 8 Ar-H), 8.15 (dd, 1H, H-5, J = 6.0, 1.5 Hz), 9.98 (s, 1H, NH).

It is noteworthy that we succeeded to prepare the 4-quinolone moiety from amidine **5a** and dimethyl 2-methoxycarbonylmalonate to reveal methyl 4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate **8** in good yield (Scheme 2).

We have mentioned the synthesis of compound **4a—d** from cyclic amidine **1** and AME's **2**. In addition, we also synthesized compounds **4a**,**b**,**e—h** via an independent route



Scheme 2.



Scheme 3.

involving reflux of the appropriate diethyl malonate **3b—e** with the amidine **1a,b** in tetralin to afford an isolable product **4** (Scheme 4, method B). The latter was found to be identical in all aspects (mp, TLC, and IR data) with that obtained via method A (Scheme 1).

Our work also dealt with synthesis of bicyclic mesoions from 2,6-bis(substituted amino)-4-methylthio-1,3,5-triazines **9**. Thus, the reaction of **9a,b** as 1,3-binucleophile with 1,3-bielectrophilic AME's **2a,c,f** furnished **10a—e** in excellent yield (Scheme 4).

The analytical and spectroscopic data are consistent with the proposed structure **10**. For example, compound **10d** showed IR absorption peaks at ν_{max} 3300 (NH), 1689 and 1661 cm^{-1} (CO); ^1H NMR ($CDCl_3$) revealed δ = 1.06 (t, 3H, CH_3, J = 7 Hz), 1.30, 1.56 (each d, each 6H, 2×CH_3, J = 6 Hz), 2.43 (q, 2H, CH_2, J = 7.5 Hz), 2.55 (s, 3H, SCH_3), 4.26, 5.62 (each q, each 1H, CH, J = 6.5 Hz), 12.72 (d, 1H, NH, J = 7 Hz).

This investigation has been extended to consider cycloaddition reactions of the mesoion **6**. The dipolar character of mesoion **6** may be envisaged as 1,4-dipolar systems. In such a light, it appears to be a good candidate for [4+2] cycloaddition reactions. Thus, compounds **6c,d** were allowed to react with equimolar amounts of maleic anhydride or *N*-phenylmaleimide for a few minutes to furnish the corresponding 1 : 1 cycloadducts **11c,d** and **13c,d**, respectively.

The spectroscopic data are consistent with those found in other 2,6-diazabicyclo[2.2.2] ring systems.[1,21] Thus, the IR spectrum of **13d** revealed absorption bands at ν_{max} 1788, 1726, and 1685 cm^{-1} (CO), while ^1H NMR showed δ = 3.73 (s, 2H, CH_2-benzyl), 4.18, 5.36 (each d, each 1H, H-7, H-8, J = 8 Hz), 6.75—7.82 (m, 25 Ar-H); ^{13}C NMR showed δ = 32.5 (C-11), 41.5 (C-7), 51.8 (C-8), 56.82 (C-4), 83.2 (C-1), 167.5 (C-9), 167.8 (C-10), 172.6 (C-3), 172.7 (C-5).

Interestingly, upon refluxing the diphenyl ether solution of **11d** in the presence of palladium/charcoal, it underwent aromatization via an intramolecular ring transformation along with the elimination of carbon dioxide and toluene. This ring transformation furnished 2,5,6-triphenyl-1*H*-pyrrolo[3,4-*c*]pyridine-1,3,4(2*H*,5*H*)-trione **12**. The latter structure was substantiated by elemental analysis and spectroscopic data. Thus, ^{13}C NMR showed δ = 100.4 (C-f), 114.1 (C-c), 131.5 (C-g), 134.5 (C-j), 137.7 (C-i), 145.4 (C-h), 155.6 (C-d), 159.8 (C-e), 165.0 (C-b), 165.3 (C-a). ^1H NMR showed beside the three phenyls protons (15 H) signal at δ = 7.20—7.90, singlet signal at δ = 6.82 corresponding to one proton at C-7. In addition, a lack of the characteristic CH_2-benzyl protons, indicating that toluene was eliminated through a ring transformation, was consistent with our product **12**.

It is noteworthy that a ring transformation could occur only under controlled conditions, leading to heterocycles, which are often difficult to obtain by alternative routes. Thus, although the primary adducts, **11c** or **13c,d**, were already isolated (quite stable) when subjected to the same reaction conditions as applied for **11d**, we could not succeed to obtain product **12** (Scheme 5).

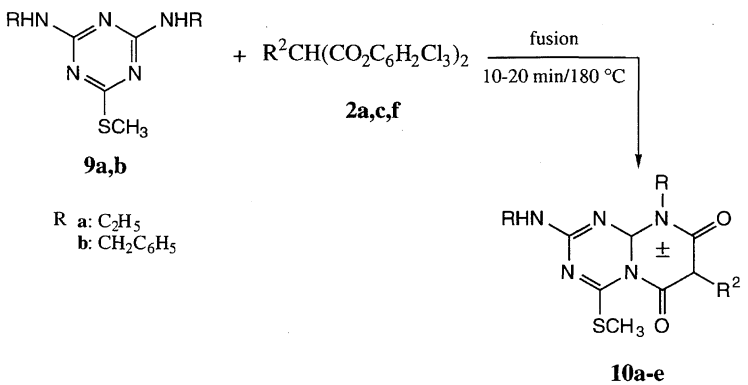
Scheme 6 depicts the 1,4-dipolar cycloaddition of dimethyl acetylenedicarboxylate (DMAD) to the mesoion **6b,c**, where the primary adduct **14b,c** formed as an intermediate, which simultaneously rearranged to 2-pyridones **15b,c** via a loss of phenyl isocyanate. It is noteworthy that similar cycloaddition reactions have been reported, and in a few cases the primary adduct was isolated and fully characterized.[1] Alkaline hydrolysis of the ester **15c** achieved the dicarboxylic acid **16c**. Thus, the mass spectrum of **16c** revealed the molecular ion peak at m/z 345 (M^+-18; 18%) corresponding to the molecular formula $C_{21}H_{17}NO_5$.

The analytical and spectral data of the newly synthesized compounds are tabulated in Tables 1, 2, 3, and 4 in addition to that in the experimental part.

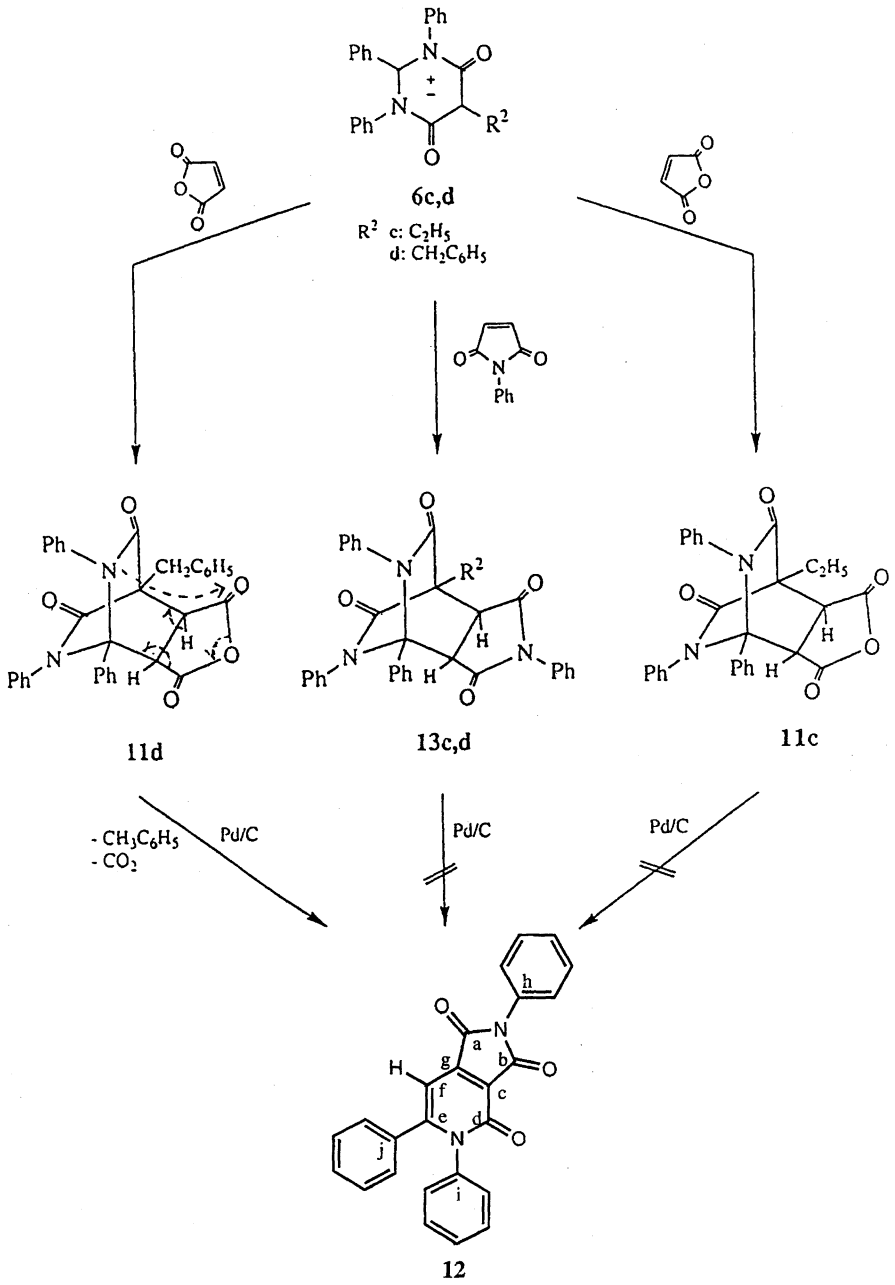
As a conclusion, the results obtained in this work have demonstrated a simple methodology for the construction of a wide variety from heterocycles of pyrimidine systems, obtainable only with difficulty otherwise, in addition to their prospective wide spectrum of potential bioresponses.

Experimental

Melting points were determined on a Gallenkamp apparatus and are uncorrected. The IR spectra were taken in potassium bromide on Perkin Elmer 398 spectrophotometer; ^1H NMR and ^{13}C NMR were recorded on a Bruker WM 300 spectrometer. The solvent for the NMR spectra was DMSO-d_6, unless otherwise stated. Mass spectra were obtained on a Shimadzu, GC MS. QP 1000Ex mass spectrometer (70 eV EI mode); elemental analyses were accomplished with a Carlo Erba 1106 CHN analyzer. Common reagent-grade, commercially available materials were used without further



Scheme 4.



Scheme 5.

purification or being prepared by standard literature procedures. All of the reactions were monitored by thin-layer chromatography, and carried out on 0.2 mm silica-gel 60 F-254 (Merck) plates using UV light for detection.

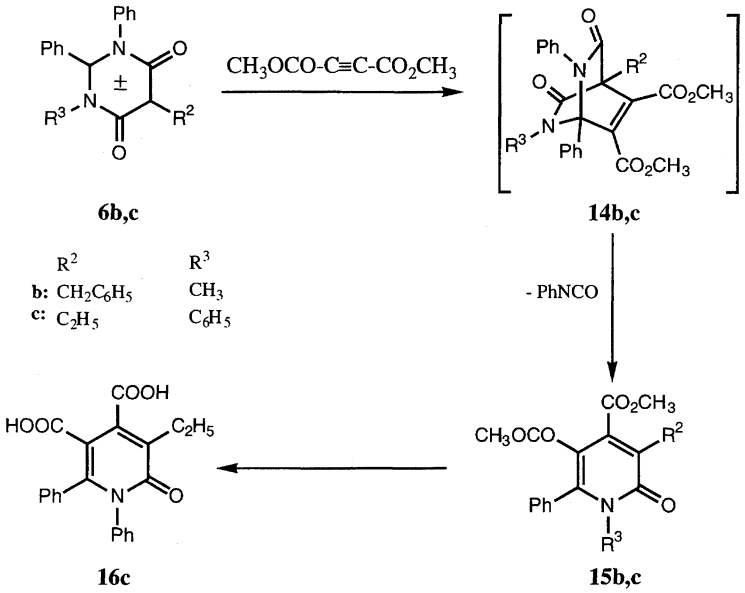
General Method for Preparation of 4-Oxo-4*H*-pyrido[1,2-*a*]-pyrimidin-1-ium-2-olate (4a—h).

Method A (4a—d). A mixture of 2-(substituted amino)pyridine **1a,b** (10 mmol) and substituted bis-2,4,6-trichlorophenyl (2-substituted) malonate **2a,c** (10 mmol) was fused for 5—10 min at 175—190 °C. The oily residue was digested with 20 ml diethyl ether. The precipitate was collected by suction and washed with cyclohexane (data, see Tables 1 and 4).

Method B (4a, b, e—h). A mixture of 2-(substituted amino)-pyridine **1a,b** (10 mmol), corresponding diethyl malonate **3b—e** (11 mmol) and tetraline (5 ml) was refluxed for 2—6 h. After cooling, the resulting oily product was digested with cyclohexane; the precipitate was collected by suction filtration and washed with petroleum ether (data see Tables 1 and 4).

5-Butyl-3,4-dihydro-4-oxo-1,2,3-triphenylpyrimidin-1-ium-6-olate (6a). *N,N′*-Diphenylbenzamidine **5a** (2.72 g; 10 mmol) and bis(2,4,6-trichlorophenyl) 2-butylmalonate (5.16 g; 10 mmol) were fused for 10 min at 175 °C and worked up according to the preparation of **4**, method A. Yield (2.91 g; 73%). Mp 267—268 °C (from toluene); IR (KBr) 1645—1660 cm^{-1} (CO); ^1HNMR ($CDCl_3$) δ = 0.93 (t, 3H, CH_3, J = 8 Hz), 1.38—1.71 (m, 4H, 2×CH_2), 2.58 (t, 2H, CH_2, J = 7.5 Hz), 6.98—7.27 (m, 15 Ar–H). Found: C, 79.01; H, 6.06; N, 7.07%. Calcd for $C_{26}H_{24}N_2O_2$: C, 78.76; H, 6.10; N, 7.07%.

5-Benzyl-3,4-dihydro-1-methyl-4-oxo-2,3-diphenylpyrimidin-1-ium-6-olate (6b). A mixture of *N*-methyl-*N′*-phenylbenzamidine **5b** (2.10 g; 10 mmol) and bis(2,4,6-trichlorophenyl) 2-benzylmalonate **2f** (5.8 g; 10 mmol) was fused for 7 min at 180



Scheme 6.

Table 1. Yield and Analytical Characterization of Compounds **4a—h**

Cpd	···4-Oxo-4*H*-pyrido [1,2-*a*]pyrimidin-1-ium-2-olate	Reaction time Temp/°C	Method: Yield/%	Mp/°C Recryst. solvent	Molecular formula M. Wt	Analysis/%, Calcd/Found		
						C	H	N
4a	3-Butyl-1-methyl-	10 min/175	A : 90	149—150	$C_{13}H_{16}N_2O_2$	67.21	6.96	12.06
		4 h	B : 27	Xylene	232.30	66.9	6.89	11.92
4b	1-Benzyl-3-butyl-	5 min/180	A : 76	137—138	$C_{19}H_{20}N_2O_2$	74.00	6.54	9.08
		4 h	B : 24	EtOH : cyclohex. (2 : 1)	308.42	73.80	6.45	9.01
4c	1-Benzyl-3-ethyl-	5 min/180	A : 86	175—176	$C_{17}H_{16}N_2O_2$	72.84	5.75	9.99
				Toluene	280.36	72.65	5.81	9.88
4d	3-Ethyl-1-methyl-	5 min/190	A : 87	229—230	$C_{11}H_{12}N_2O_2$	64.69	5.92	13.72
				MeOH	204.25	64.88	6.00	13.74
4e	1-Methyl-3-phenyl	6 h	B : 38	200—201	$C_{15}H_{12}N_2O_2$	71.42	4.79	11.10
				Xylene	252.30	71.59	4.76	11.09
4f	1-Benzyl-3-phenyl-	2 h	B : 36	264—265	$C_{21}H_{16}N_2O_2$	76.81	4.91	8.53
				Toluene	328.40	76.50	4.96	8.40
4g	3-Allyl-1-benzyl-	6 h	B : 58	84—85	$C_{18}H_{16}N_2O_2$[b]	77.81	5.99	7.56
				Benzene	292.34	77.66	5.95	7.77
4h	1-Benzyl-3-(2-cyanoethyl)-	4 h	B : 42	187—188[a]	$C_{18}H_{15}N_3O_2$	70.79	4.96	13.76
				Acetone	305.37	70.44	5.24	13.39

a) Column chromatography (chloroform : acetone) 9 : 1 as eluent then recrystallized from acetone. b) Calculated $C_{18}H_{16}N_2O_2$+1 C_6H_6.

Table 2. Yield and Analytical Characterization of Quinolones **7a—e** and **8**

Cpd	···2-Phenyl-4-quinolone except **8**	Reaction time h	Yield %	Mp/°C Recryst. solvent	Molecular formula M. Wt	Analysis/% Calcd/Found		
						C	H	N
7a	3-Butyl-	2	65	196—197	$C_{19}H_{19}NO$	82.28	6.90	5.05
				EtOH	277.36	82.33	6.93	4.97
7b	3-Ally-	4	61	218—219	$C_{18}H_{15}NO$	82.73	5.79	5.36
				Acetonitrile	261.32	82.72	5.70	5.47
7c	3-(2-Cyanoethyl)-	4	52	271—273	$C_{18}H_{14}N_2O$	78.18	5.14	10.21
				BuOH	274.33	77.94	5.06	10.02
7d	3-Phenyl-	2	81	337—338[a]	$C_{21}H_{15}NO$	84.85	5.09	4.71
				Acetone	297.39	84.95	5.05	4.65
7e	3-(3-Cyanopropyl)-	3	78	203—204	$C_{19}H_{15}N_2O$	79.42	5.26	9.75
				Acetonitrile	287.34	79.42	5.44	9.75
8	Methyl 4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate	4	87	247—248	$C_{17}H_{13}NO_3$	73.11	4.69	5.01
				Acetonitrile	279.30	73.15	4.75	4.96

a) Column chromatography (chloroform : acetone) 9 : 1 as eluent then recrystallized from acetone.

Table 3. Yield and Analytical Characterization of Compounds **10a—e**

Cpd	···amino-4-methylthio-6-oxo-6*H*-pyrimido[1,2-*a*]-1,3,5-triazin-9-ium-8-olate	Reaction time min	Method: Yield %	Mp/°C Recryst. solvent	Molecular formula M. Wt	Analysis/% Calcd/Found C	H	N
10a	7,9-Diethyl-2-ethyl	10	A : 92	145—146[a] Acetonitrile	$C_{13}H_{19}N_5O_2S$ 309.39	50.47 50.30	6.19 6.14	22.64 22.75
10b	7-Butyl-9-ethyl-2-ethyl	12	A : 95	101—102 Acetonitrile	$C_{15}H_{23}N_5O_2S$ 337.45	53.39 53.40	6.87 6.85	20.75 20.36
10c	7-Benzyl-9-ethyl-2-ethyl	15	A : 76	165—167[b] Acetone	$C_{18}H_{23}N_5O_2S$ 371.46	58.20 58.60	5.70 6.02	18.85 18.48
10d	7-Ethyl-9-isopropyl-2-isopropyl	15	A : 62	162—163 Toluene	$C_{15}H_{23}N_5O_2S$ 337.45	53.39 53.42	6.87 6.92	20.75 20.89
10e	7-Benzyl-9-isopropyl-2-isopropyl	20	A : 68	152—154 Cyclohex.	$C_{20}H_{25}N_5O_2S$ 339.52	60.13 59.77	6.31 6.36	17.53 17.55

a) Column chromatography (chloroform : acetone) 9 : 1 as eluent, then recrystallized from acetonitrile. b) Column chromatography (chloroform : acetone) 9 : 1 as eluent, then recrystallized from acetone.

Table 4. IR (cm^{-1}) and ^1H NMR (ppm) Spectroscopic Data for Selected Mesoions **4**, **7**, **8**, and **10**

Cpd	IR/cm^{-1}	^1H NMR paramter
4a	1680, 1640—1626	0.92 (t, 3H, CH_3, J = 7 Hz), 1.22—1.53 (m, 4H, CH_2CH_2), 2.48 (t, 2H, CH_2, J = 7 Hz), 3.66 (s, 3H, N–CH_3), 7.48 (t, 1H, H-7, J = 6.5 Hz), 7.82 (dd, 1H, H-9, J = 8.5, 1.5 Hz), 8.28 (t, 1H, H-8, J = 6 Hz), 9.22 (dd, 1H, H-6, J = 7, 2 Hz).
4g	1689, 1642—1630	3.24 (d, 2H, CH_2, J = 6 Hz), 4.86—4.20 (m, 2H, CH_2=), 5.56 (s, 2H, CH_2–benzyl), 5.82—6.01 (m, 1H, CH=), 7.28—7.38 (m, 5Ar–H), 7.48 (t, 1H, H-7, J = 7 Hz), 7.63 (dd, 1H, H-9, J = 9, 1.5 Hz), 8.21 (t, 1H, H-8, J = 8 Hz), 9.25 (dd, 1H, H-6, J = 6, 1.5 Hz).
4h	2221, 1686, 1642—1625	2.55 (t, 2H, CH_2, J = 7 Hz), 2.82 (t, 2H, CH_2, J = 7 Hz), 5.56 (s, 2H, CH_2–benzyl), 7.30 (s, 5Ar–H), 7.50 (t, 1H, H-7, J = 7 Hz), 7.66 (d, 1H, H-9, J = 6 Hz), 8.28 (t, 1H, H-8, J = 6.5 Hz), 9.27 (dd, 1H, H-6, J = 5, 1.4 Hz).
7b	3032, 1630, 1589, 1549, 1502	3.12 (d, 2H, CH_2, J = 5 Hz), 4.72—4.87 (m, 2H, CH_2=), 5.75—5.96 (m, 1H, CH=), 7.28—7.73 (m, 8Ar–H), 8.14 (dd, 1H, H-5, J = 6, 1.7 Hz), 11.70 (s, 1H, NH).
7c	3095, 2223, 1629, 1582, 1550, 1510	2.63 (t, 2H, CH_2, J = 7 Hz), 2.77 (t, 2H, CH_2, J = 7 Hz), 7.32—7.78 (m, 8Ar–H), 8.19 (dd, 1H, H-5, J = 6, 1.5 Hz), 11.87 (s, 1H, NH).
8	3108, 1722, 1625, 1602, 1575, 1519	3.45 (s, 3H, CH_3), 7.34—7.78 (m, 3H, H-6, H-7, H-8), 7.56 (s, 5Ar-H), 8.12 (dd, 1H, H-5, J = 6, 1.5 Hz), 12.11 (s, 1H, NH).
10a	3292, 1681, 1643	a) 1.05 (t, 3H, CH_3, J = 6.5 Hz), 1.22—1.32 (m, 2 × CH_3), 2.43 (q, 2H, CH_2, J = 6.5 Hz), 2.53 (s, 3H, SCH_3), 3.58, 4.29 (each q, 2H, each CH_2, J = 7 Hz), 12.73 (t, 1H, NH, J = 4 Hz).
10e	3288, 1680, 1645	a) 1.30, 1.50 (each d, 6H, each 2 × CH_3, J = 6 Hz), 2.54 (s, 3H, SCH_3), 3.70 (s, 2H, CH_2), 4.26, 5.78 (each q, 1H, each CH, J = 6.5 Hz), 7.12—7.42 (m, 5Ar–H), 12.62 (d, 1H, NH, J = 7 Hz).

a) If indicated, deuteriochloroform was used as the solvent.

°C and worked up analogous to **6a**. Yield (2.61 g; 71%). Mp 235—236 °C (from benzene–cyclohexane) (3 : 1); IR 1645 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ = 3.25 (s, 3H, N–CH_3), 3.85 (s, 2H, CH_2–benzyl), 6.80—7.65 (m, 15Ar–H). Found: C, 78.46; H, 5.57; N, 7.67%. Calcd for $C_{24}H_{20}N_2O_2$: C, 78.26; H, 5.43; N, 7.61%.

5- Ethyl or Benzyl- 3, 4- dihydro- 4- oxo- 1, 2, 3- triphenylpyrimidin-1-ium-6-olate (6c,d) according to Ref. 21.

General Method for Preparation of 2-Phenyl-4-quinolones (7a—d). A mixture of *N,N'*-diphenylbenzamidine **5a** (2.72 g; 10 mmol) and diethyl (2-substituted) malonate **3b—e** (10 mmol) was worked up according to the preparation of **4**, method B. (data, see Tables 2 and 4).

3-(3-Cyanopropyl)-2-phenyl-4-quinolone (7e). Compound **5a** (2.72 g; 10 mmol) and dimethyl 2-(3-cyanopropyl) malonate **3g** (1.9 g; 10 mmol) were worked up according to the preparation of **7a—d** (data, see Table 2).

Methyl 4-Oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate (8). From **5a** (2.72 g; 10 mmol) and dimethyl 2-methoxycarbonyl malonate (1.9 g; 10 mmol), then, according to **7a—e** (data, see Tables 2 and 4).

General Method for Preparation of 4-Methylthio-6-oxo-6*H*-pyrimido[1.2-*a*]-1,3,5-triazin-9-ium-8-olate (10a—e). A mixture of the corresponding 2,6-bis(substituted amino)-4-methylthio-1,3,5-triazines **9a,b** (10 mmol) and **2a,c,f** (10 mmol) was fused at 180 °C for the time given in Table 3 and then worked up according to the preparation of **4**, method A. (data, see Tables 3 and 4).

4-Ethyl-3,5-dioxo-1,2,6-triphenyl-2,6-diazabicyclo[2.2.2]octane-7,8-dicarboxylic Anhydride (11c). Compound **6c** (0.92 g; 2.5 mmol) was fused with maleic anhydride (0.25 g; 2.5 mmol) for 15 min at 175 °C; the resulting residue was digested with cy-

clohexane, then petroleum ether, to yield (0.61 g; 53%). Mp 238—240 °C (from chlorobenzene); IR 1775, 1705, 1670 cm^{-1} (CO); ^1H NMR δ = 1.20 (t, 3H, CH_3, J = 8 Hz), 2.40 (q, 2H, CH_2, J = 8 Hz), 4.50, 5.75 (each d, each 1H; H-7, H-8, J = 10 Hz); 6.61—7.52 (m, 15 Ar–H). Found: C, 72.10; H, 4.81; N, 6.04%. Calcd for $C_{28}H_{22}N_2O_5$: C, 72.09; H, 4.75; N, 6.01%.

2,5,6-Triphenyl-1*H*-pyrrolo[3,4-*c*]pyridine-1,3,4-(2*H*,5*H*)-trione (12). 4-Benzyl-3,5-dioxo-1,2,6-triphenyl-2,6-diazabicyclo-[2.2.2]octane-7,8-dicarboxylic anhydride **11d** (0.52 g; 1 mmol) was refluxed for 16 h in 10 ml diphenyl ether containing palladium–charcoal as a catalyst (ca. 10 mg); after cooling, the mixture was diluted with benzene, and the catalyst was separated; petroleum ether was added to the filtrate to yield (0.29 g; 78%). Mp 174—175 °C (from benzene); IR 1775, 1720, 1640 cm^{-1} (CO); ^1H NMR δ = 6.80 (s, 1H), 7.21—7.93 (m, 15 Ar–H); ^{13}C NMR δ = 100.4 (C-f), 114.1 (C-c), 131.5 (C-g), 134.5 (C-j), 137.7 (C-i), 145.4 (C-h), 155.6 (C-d), 159.8 (C-e), 165.0 (C-b), 165.3 (C-a). Found: C, 76.65; H, 4.20; N, 6.91%. Calcd for $C_{25}H_{16}N_2O_2$: C, 76.52; H, 4.11; N, 7.14%.

4-Ethyl-3,5-dioxo-1,2,6-triphenyl-2,6-diazabicyclo[2.2.2]octane-7,8-dicarboxylic *N*-Phenylimide (13c). Compound **6c** (0.92 g; 2.5 mmol) was fused with *N*-phenylmaleimide (0.44 g; 2.5 mmol) for 15 min at 180 °C and then worked up according to the preparation of **11c**. Yield (0.93 g; 69%). Mp 270—271 °C (from toluene); IR 1781, 1722, 1680 cm^{-1} (CO); ^1H NMR δ = 1.29 (t, 3H, CH_3, J = 6 Hz); 2.0 (q, 3H, CH_3, J = 8 Hz), 4.21, 5.38 (each d, each 1H, H-7, H-8, J = 8.6 Hz), 6.70—7.61 (m, 20 Ar–H). Found: C, 75.02, H, 5.01; N, 7.43%. Calcd for $C_{34}H_{27}N_3O_4$: C, 75.40; H, 5.02; N, 7.76%.

4-Benzyl-3,5-dioxo-1,2,6-triphenyl-2,6-diazabicyclo[2.2.2]octane-7,8-dicarboxylic *N*-Phenylimide (13d). Compound **6d** (1.08 g; 2.5 mmol) was fused with *N*-phenylmaleimide (0.44 g; 2.5 mmol) for 15 min at 185 °C; the resulting oily product was subjected to column chromatography using chloroform–acetone (3 : 7) as an eluent to yield (1.08 g; 72%). Mp 290—291 °C (from toluene); IR 1788, 1726, 1685 cm^{-1} (CO); ^1H NMR δ = 3.73 (s, 2H, CH_2–benzyl) 4.18, 5.36 (each d, each 1H, H-7, H-8, J = 8 Hz), 6.75—7.82 (m, 25 Ar–H); ^{13}C NMR δ = 32.5 (C-11), 41.5 (C-7), 51.8 (C-8), 56.82 (C-4), 83.2 (C-1), 167.5 (C-9), 167.8 (C-10), 172.6 (C-3), 172.7 (C-5). Found: C, 77.42; H, 4.82; N, 6.70%. Calcd for $C_{39}H_{29}N_3O_4$: C, 77.60; H, 4.84; N, 6.96%.

Dimethyl 3-Benzyl-1-methyl-2-oxo-6-phenyl-1,2-dihydropyridine-4,5-dicarboxylate (15b). Compound **6b** (1.84 g; 5 mmol) was refluxed with dimethyl acetylenedicarboxylate (2 ml, 14 mmol), in xylene (25 ml) for 16 h. After the reaction, the solvent was evaporated in vacuo. The residue was digested several times with cyclohexane, then with petroleum ether. Yield (0.68 g; 35%); Mp 115—117 °C (from methanol); IR 1740, 1645 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ = 3.20, 3.35, (each s, each 3H, CH_3–ester), 3.75 (s, 3H, N–CH_3), 3.95 (s, 2H, CH_2–benzyl), 6.90—7.61 (m, 10 Ar–H). Found: C, 70.61; H, 5.43; N, 3.73%. Calcd for $C_{23}H_{21}NO_5$: C, 70.58; H, 5.37; N, 3.58%.

Dimethyl 5-Ethyl-6-oxo-1,2-diphenyl-1,6-dihydropyridine-3,4-dicarboxylate (15c). A mixture of **6c** (1.84 g; 5 mmol) was refluxed with dimethyl acetylenedicarboxylate (2 ml, 14 mmol) and then worked up according to **15b**. Yield (0.99 g; 46%). Mp 165—167 °C (from methanol): IR 1735, 1655 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ = 1.2 (t, 3H, CH_3–ethyl, J = 8 Hz), 2.6 (q, 2H, CH_2, J = 8 Hz), 3.35, 3.90 (each s, each 3H, CH_3– ester), 6.80—7.22 (m, 10 Ar–H). Found: C, 70.40; H, 5.43; N, 3.91%. Calcd for $C_{23}H_{21}NO_5$: C, 70.58; H, 5.37; N, 3.58%.

5-Ethyl-6-oxo-1,2-diphenyl-1,6-dihydropyridine-3,4-dicarboxylic Acid (16c). A solution of **15c** (0.5 g; 0.12 mol) in 1-propanol (10 ml) was refluxed in sodium hydroxide (50 ml) for 3 h; after cooling the solution was acidified and the organic compound was extracted with a mixture of benzene–diethyl ether (1 : 1) (50 ml). The solvent was evaporated and the residue digested with cyclohexane to yield (0.29 g; 67%). Mp 221—224 °C (from methanol); IR 3060—2960, 1740, 1630 cm^{-1} (CO); MS *m/z* 345 (M^+−18; 18%), 317 (5), 316 (6), 272 (4), 244 (2), 180 (12), 91 (10), 77 (38), 59 (16), 58 (31), 51 (16), 44 (100). Found: C, 69.69; H, 4.95; N, 3.91%. Calcd for $C_{21}H_{17}NO_5$: C, 69.41; H, 4.72; N, 3.85%.

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