CROATICA CHEMICA ACTA CCACAA **65** (4) 801–811 (1992)

ISSN 0011–1643
UDC 547
CCA—2099

Original Scientific Paper

Synthesis of Some New Condensed Heterocycles from Diethyl 2,5–Dioxocyclohexane–1,4–dicarboxylate

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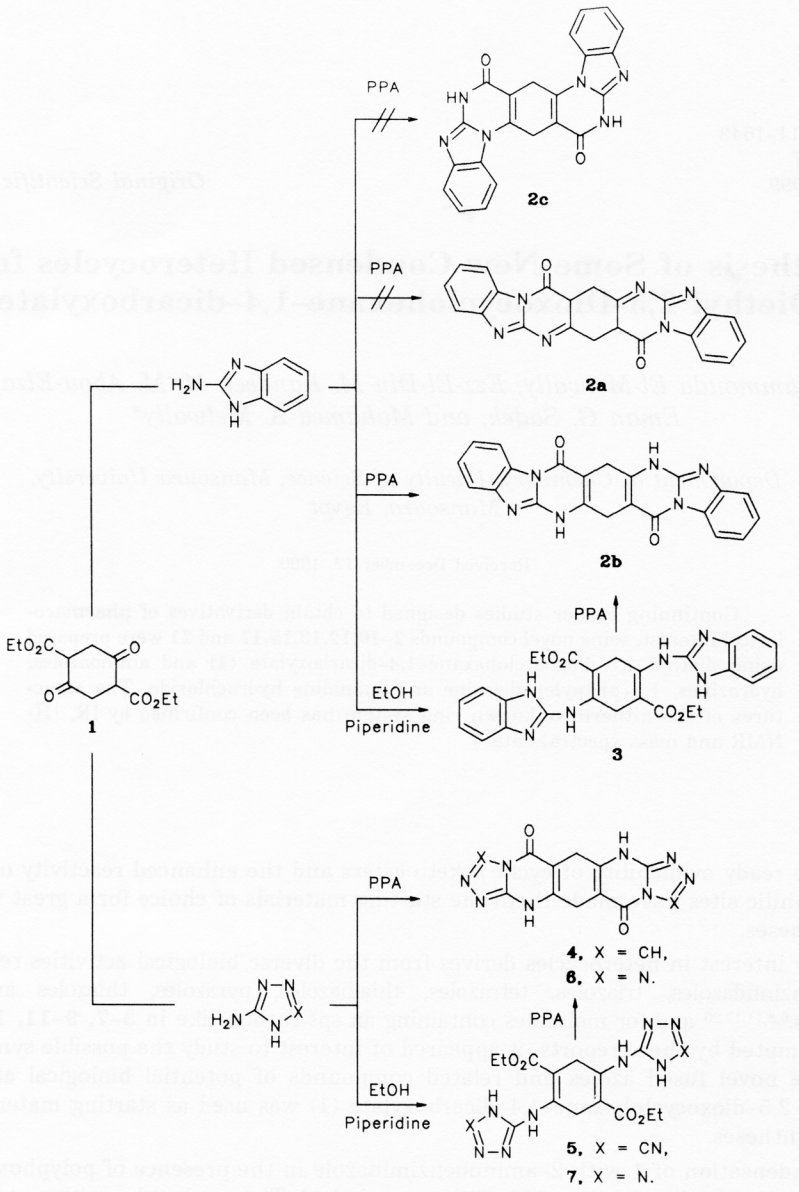
Received December 12, 1990

Continuing earlier studies designed to obtain derivatives of pharmacological interest, some novel compounds **2–10,12,13,15,17** and **21** were prepared using diethyl 2,5–dioxocyclohexane–1,4–dicarboxylate (**1**) and aminoazoles, hydrazines, 1,2–phenylenediamine and guanidine hydrochloride. The structures of the hitherto unknown ring system has been confirmed by IR, ^{1}H-NMR and mass spectral data.

The ready availability of cyclic β-keto esters and the enhanced reactivity of their electrophilic sites have made them the starting materials of choice for a great variety of syntheses.

Our interest in heterocycles derives from the diverse biological activities reported for benzimidazoles, triazoles, tetrazoles, thiadiazoles, pyrazoles, thiazoles and diazepines,[6,8,11,17,20] and for molecules containing an sp^2 carbon like in **3–7, 9–11, 18** and **22**. Prompted by these reports, it appeared of interest to study the possible syntheses of some novel fused azoles and related compounds of potential biological activity. Diethyl 2,5–dioxocyclohexane–1,4–dicarboxylate (**1**) was used as starting material for their syntheses.

Condensation of **1** with 2–aminobenzimidazole in the presence of polyphosphoric acid gave the product (m.p. > 300 °C) in a good yield. The product has either structure **2a**, **2b** or **2c** consistent with the molecular formula $C_{22}H_{14}N_6O_2$ as obtained by elemental analysis and mass spectrometry. The spectrum of this product showed NH and carbonyl absorptions at 3150 and 1660 cm^{-1}, respectively, and thus favours structure **2b**. The assignment of the linear structure **2b** is also consistent with the observations made in previous publications.[14,15,16] The mass spectrum of **2b** gave an M^+ at m/z 394 which agrees with the molecular formula of $C_{22}H_{14}N_6O_2$. Further evidence for the structure of **2b** was gained by treatment of **1** with 2–aminobenzimidazole in ethanol/piperidine



Scheme 1.

to give the anil product **3** (Scheme 1). Compound **3** upon treatment with polyphosphoric acid afforded the product having a mass spectrum and m.p. identical to **2**. The formation of **3** proceeds in the usual manner for the interaction of **1** with aromatic amines.[9] No molecular ion was observed in the mass spectrum of **3** but the fragment

at m/z 254 corresponding to $C_{12}H_{18}N_2O_4$ was obviously formed by loss of two benzimidazole fragments from the parent ion.

Following the above condensation procedure, **1** treated with 3–amino–1,2,4–triazole in polyphosphoric acid gave **4**. The assignment of structure **4** was based on the IR and mass spectral data (*cf.* Table I and II). Moreover, condensation of **1** with the same reagent in ethanol/piperidine afforded the anil product **5**, which underwent cyclization with polyphosphoric acid to **4** (Scheme 1). Structure **5** was confirmed by elemental analysis, IR and ^{1}H-NMR spectra (*cf.* Tables I and II).

In connection with the above reaction, it also seemed of interest to react 5–aminotetrazole monohydrate with **1** in polyphosphoric acid to give **6**. In addition to the correct analytical and spectral data, further support for the structure of **6** was gained by treating **1** with 5–aminotetrazole in ethanol/piperidine to give the corresponding anil

TABLE I

Characterization data of compounds ***2b,3–10,12,13*** *and* ***15.***

Compd. no.	M.p. °C	Yield %	Colour	Mol. Formula (Mol. wt.)	IR cm^{-1}	Analysis					
						Calcd.			Found		
						C	H	N	C	H	N
2b	>300	60	G.Y.	$C_{22}H_{14}N_6O_2$ (394.38)	1660, 1595, 3215	66.99	3.57	21.31	66.83	3.79	21.51
3	>300	70	Y.	$C_{26}H_{26}N_6O_4$ (486.52)	3250, 1689. 1610	64.18	5.38	17.27	64.39	5.21	17.11
4	>300	70	P.Y.	$C_{12}H_8N_8O_2$ (296.24)	1670, 1635, 3210	48.64	2.72	37.82	48.81	2.55	38.01
5	122	85	Y.	$C_{16}H_{20}N_8O_4$ (388.39)	3290, 1680 1620	49.47	5.19	28.85	49.69	5.39	29.01
6	>300	65	G.B.	$C_{10}H_6N_{10}O_2$ (298.22)	1690, 1610 1620, 1630	40.27	2.02	46.97	39.92	2.13	47.11
7	122	80	Y.	$C_{14}H_{18}N_{10}O_4$ (390.36)	3250, 1685, 1580	43.07	4.64	35.88	43.19	4.73	36.01
8	165	75	D.B.	$C_{30}H_{30}N_6O_6$ (570.59)	3250, 1690, 1660, 1595	63.14	5.3	14.73	63.21	5.29	14.89
9	177	80	D.B.	$C_{30}H_{30}N_6O_4$ (538.59)	3360, 1700, 1600, 3310	66.89	5.61	15.6	66.93	5.79	15.81
10	165	65	D.O.	$C_{34}H_{40}N_8O_6$ (657.52)	3400, 1690, 1665, 1600	62.1	6.13	17.16	62.31	6.01	17.39
12a	>300	85	Y.B.	$C_{18}H_{14}N_6O_2$ (346.34)	3225, 1665	62.41	4.07	24.27	62.31	3.91	24.39
12b	125	75	D.O.	$C_{22}H_{16}N_4S_2O_{12}$ (592.51)	3100, 1680, 1660	44.59	2.72	9.45	44.69	2.51	9.39
13	220	80	P.Y.	$C_{36}H_{38}N_4S_4O_{12}$ (844.94)	3200, 1680, 1655	51.17	4.29	6.63	51.01	4.36	6.5
15a	>300	90	D.R.	$C_{20}H_{14}N_6O_6$ (434.36)	3350, 1660, 1590	55.29	3.24	19.35	55.43	3.39	19.11
15b	203	70	B.	$C_{20}H_{14}N_4O_2Cl_2$ (413.25)	3320, 1680, 1595	58.12	3.41	13.55	57.91	3.31	13.25
15c	270	65	B.	$C_{22}H_{20}N_4O_2$ (372.41)	3315, 1670 1605	70.94	5.41	15.04	71.11	5.32	14.93
17	123	60	B.	$C_{18}H_{12}N_4O_4$ (348.31)	3320, 1680, 1640	62.06	3.47	16.08	61.93	3.35	16.31
21*	>300	75	P.Y.	$C_{10}H_{12}N_6O_2Cl_2$ (319.16)	3400, 2800, 2700, 1650, 1540, 1500.	37.67	3.79	26.33	37.91	3.86	26.39

G.Y. = Greenish yellow, Y = Yellow, P.Y. = Pale-yellow, G.B. = Greenish brown, D.B. = Deep brown, D.O. = Deep orange, Y.B. = Yellow brown, D.R. = Deep red, B. = Brown.

* Cl% Calcd. 22.21, Found 22.39.

TABLE II

^{1}H-NMR (400 MHz) of compounds ***2—10, 12, 15*** *and* ***17***

Compound no.	^{1}H-NMR
2b	1.69 (s, 2H, NH), 3.45 (s, 4H, CH_2), 6.75–7.7 (m, 8H, ArH).
3	1.45 (t, 3H, CH_3 : J = 7 Hz), 1.62 (s, 2H, NH), 3.49 (s, 4H, CH_2, cyclohexadienic), (q, 4H, CH_2 : J = 7 Hz). 10.05 (s, 2H, NH), 6.8–7.9 (m, 8H, ArH).
4	1.49 (s, 2H, NH), 3.39 (s, 4H, CH_2), 7.35 (s, 2H, olefinic triazole).
5	1.42 (t, 3H, CH_3 : J = 7 Hz), 1.57 (s, 2H, NH), 3.18 (s, 2H, CH_2, cyclohexadienic), 4.42 (q, 2H, CH_2 : J = 7 Hz), 7.48 (s, 1H, olefinic triazole) and 10.14 (s, 1H, NH).
6	1.49 (s, 2H, NH), 3.41 (s, 4H, CH_2).
7	1.42 (t, 3H, CH_3 : J = 7 Hz), 1.65 (s, 2H, NH) 3.45 (s, 4H, CH_2, cyclohexadienic), 4.45 (q, 2H, CH_2 : J = 7 Hz) 10.1 (s, 2H, NH).
8	1.45 (t, 3H, CH_3 : J = 7 Hz), 1.69 (s, 2H, NH), 3.39 (s, 4H, CH_2, cyclohexadienic) 3.95 (s, 4H, CH_2 pyrazolone), 4.39 (q, 2H, CH_2 : J = 7 Hz), 6.9–7.8 (m, 10H, ArH).
9	1.3 (m, 6H, CH_3), 4.41 (m, 4H, CH_2), 1.67 (s, 2H, NH), 13.1 (s, 2H, NH pyrazole), 3.46 (s, 4H, CH_2, cyclohexadienic), 5.7 (s, 2H, CH pyrazolic), 7.1–7.8 (m, 10H, ArH).
10	1.65 (s, 2H, NH), 3.45 (s, 4H, CH_2), 2.3 (s, 6H, CH_3), 2.4 (s, 6H, CH_3), 6.8–7.65 (m, 10H, ArH).
12a	1.27 (s, 2H, NH), 3.45 (s, 4H, CH_2, cyclohexadienic), 7.4–7.9 (m, 8H, ArH).
12b	1.61 (s, 2H, NH), 3.42 (s, 4H, CH_2, cyclohexadienic), 7.2–7.85 (m, 6H, ArH), 11.2 (s, 1H, SO_2OH) 12.3 (s, 1H, COOH).
15a	1.61 (s, 2H, methine), 3.41 (s, 4H, CH_2 cvyclohexane), 6.9–7.8 (m, 6H, ArH), 10.2 (s, 2H, NH).
17	3.41 (s, 4H, CH_2, cyclohexadienic), 9.3 (s, 2H, OH), 7.4–7.8 (m, 6H, ArH).

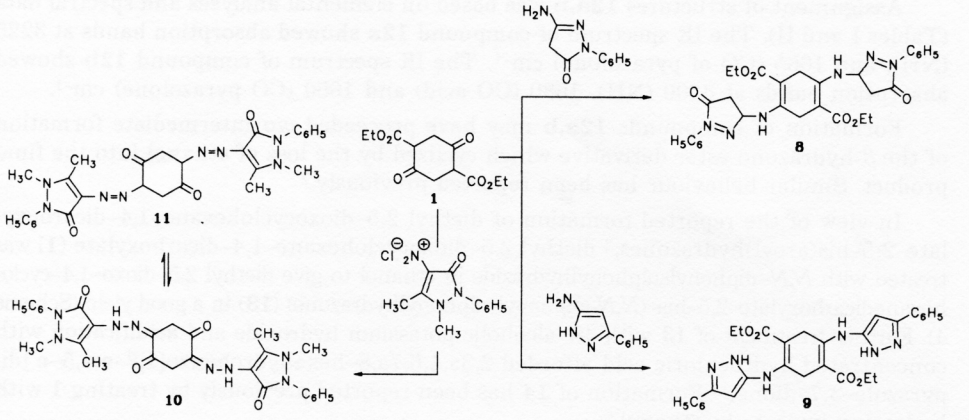
derivative **7**, which underwent subsequent cyclization in polyphosphoric acid to a product identical to **6**. The structure of **7** was confirmed by its IR and mass spectral data (*cf.* Tables I and II). As observed for **3**, also no molecular ion was observed in the mass spectrum of **7**. However the fragment present at m/z 254 which corresponds to $C_{12}H_{18}N_2O_4$, is likely to be formed by loss of two tetrazole fragments from the parent ion.

It was reported that the substitution on carbon–4 of phenazone increased the analgesic and antipyretic activity of such compounds.[4] Also the presence of substituted amino group potentiates this activity.[14,15]

TABLE III

Mass spectral data of compounds ***2b, 3, 4, 7, 8, 15a*** *and* ***21***

Compd. no.	Mass spectra m/z (rel. int)
2b	394[M]$^+$ (2), 239 (2), 265 (2), 237 (18), 235 (24), 208 (100), 170 (20).
3	253 [M–$C_{14}H_8N_4$]$^+$ (22), 208 (100), 162 (92), 133 (22).
4	296 [M$^+$], 246 (4), 216 (8), 145 (18), 91 (50), 60 (100).
7	254[M–$C_2H_2N_8$]$^+$ (26), 208 (100), 180 (40), 162 (90).
8	324 [M–$C_{16}H_{22}O_2$]$^+$ (1), 277 (1), 254 (24), 208 (100), 180 (25), 162 (75).
15a	434 [M]$^+$ (2), 375 (11), 301 (5), 166 (31), 66 (100).
21	318 [M$^+$–H] (0.5), 255 (4), 251 (20) 208 (100), 180 (30), 162 (78).

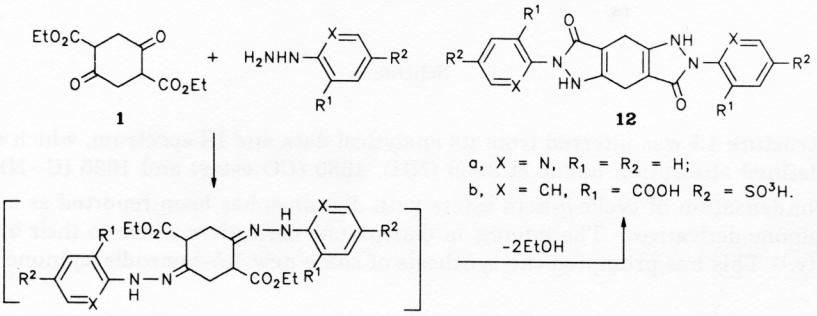


Scheme 2.

Condensation of **1** with 3–amino–1–phenyl–2–pyrazolin–5–one or 3–phenyl–5–amino-pyrazole (Scheme 2) in the presence of ethanol/piperidine resulted in the formation of bis-pyrazole derivatives **8** and **9**, respectively. Formation of **8** and **9** finds support from the spectral data (Tables I and II). In the mass spectrum of **8** (Table III) no molecular ion was observed. However, the fragment at m/z 324, corresponding to $C_{14}H_8H_6O_4$, may be formed from **8** by loss of two EtOH and C_6H_5 fragments.

It was reported earlier that **1** reacts with diazonium salts, in acetone or sodium hydroxide solution.[22] It seemed of interest to react **1** in the presence of dilute sodium hydroxide with the diazonium salt of 4–aminoantipyrine to give the bis-pyrazolone **10** or **11** (Scheme 2). From the two possible bis-pyrazolones **10** and **11**, the structure **10** was assigned to the product of the reaction since the presence of NH band in IR spectrum at 3400 cm^{-1} and NH protons in ^{1}H-NMR spectrum at δ 1.65 ppm excluded structure **11**.

As a further extension of the above reactions, treatment of compound **1** with 2–pyridylhydrazine or 2–hydrazino–5–sulphobenzoic acid gave the bis(aryl)benzo[1,2–**c**:4,5–**c'**]dipyrazole–3,7–diones **12a** and **12b** respectively (Scheme 3).

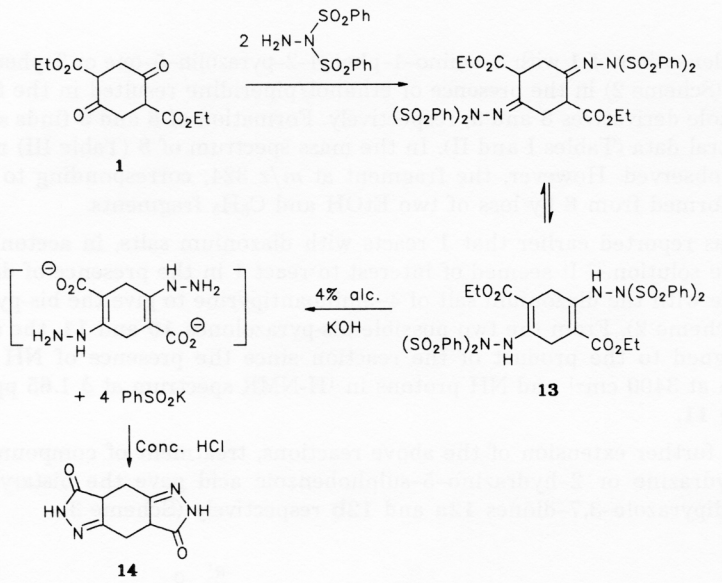


Scheme 3.

Assignment of structures **12a,b** was based on elemental analyses and spectral data (Tables I and II). The IR spectrum of compound **12a** showed absorption bands at 3225 (NH), and 1665 (CO of pyrazolone) cm^{-1}. The IR spectrum of compound **12b** showed absorption bands at 3100 (NH), 1680 (CO acid) and 1660 (CO pyrazolone) cm^{-1}.

Formation of compounds **12a,b** may have proceeded *via* intermediate formation of the β-hydrazono-ester derivative which cyclized by the loss of ethanol into the final product. Similar behaviour has been reported previously.[2]

In view of the reported formation of diethyl 2,5–dioxocyclohexane–1,4–dicarboxylate–2,5–bis(aroyl)hydrazones,[2] diethyl 2,5–dioxocyclohexane–1,4–dicarboxylate (**1**) was treated with *N,N*–diphenylsulphonylhydrazide in ethanol to give diethyl 2.5–dioxo–1,4–cyclohexanedicarboxylate–2,5–bis–(*N,N*–diphenylsulphonylhydrazone) (**13**) in a good yield (Scheme 4). Further treatment of **13** with 4% alcoholic potassium hydroxide and acidification with concentrated hydrochloric acid afforded 2,3a,4,6,7a,8–hexahydrobenzo[1,2–**c**:4,5–**c**']dipyrazole–3.7–dione.[14] Formation of **14** has been reported previously by treating **1** with hydrazine hydrate in ethanol.[2]



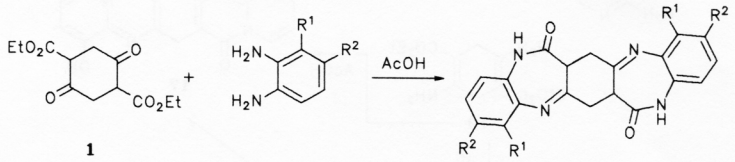
Scheme 4.

Structure **13** was inferred from its analytical data and IR spectrum, which showed well defined absorption bands at 3200 (NH), 1680 (CO ester) and 1635 (C=N) cm^{-1}.

Condensation of cyclic β-keto esters with diamines has been reported as a rout to diazepinone derivatives.[1] The interest in diazepinone derivatives is due to their biological activity.[12] This has prompted the synthesis of some new 1,5–benzodiazepinone derivatives.

Thus, condensation of diethyl 2,5–dioxocyclohexane–1,4–dicarboxylate (**1**) with 4–nitro–1,2–phenylenediamine, 4–chloro–1,2–phenylenediamine or 3–methyl–1,2–phenyl-

enediamine in hot glacial acetic acid resulted in the formation of 6,6a,8,14,14a,16–hexahydrobenzo[1,2–**b**:4,5–**b**']bis[1,5]–substitute (benzo)diazepine–7,15–diones (**15a–c**) (Scheme 5). Structures (**15a–c**) were assigned from their analytical and spectral data. The IR spectra showed absorption bands at 3400–3300 (NH), 1600–1660 (CO amide) and 1620–1590 (C=N) cm^{-1}. Also, the molecular ion (M^+) of **15a** and the obtained fragmentation support the structure **15a** (Table III).

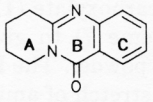


1 **15**

a, R^1 = H, R^2 = NO_2;
b, R^1 = H, R^2 = Cl;
c, R^1 = CH_3, R^2 = H.

Scheme 5.

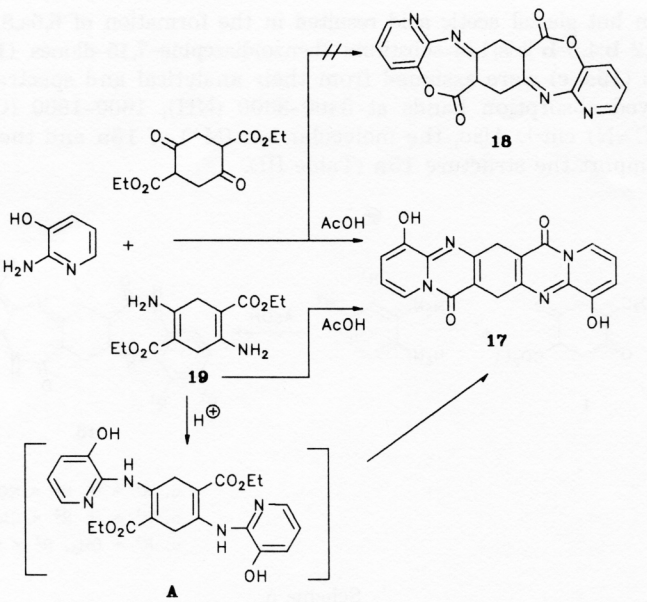
Although the pyrido[2,1–b]quinazoline moiety (**16**) is present in various alkaloids isolated from a number of plants (*Mackinlaya subulate, Mackinlaya macrosciadia, Peganum harmala, Adhatoda vasica and Evodia rutascarpa*),[3] hardly any attention has been paid to the related benzo–4H–pyrido[1,2–a]pyrimidin–9–hydroxy–4–one. Yokoyama *et al.*,[22] have reported that compound **1** reacts with 2–aminopyridine in glacial acetic acid giving pyridopyrimidoquinazolinones,. Therefore it appeared of interest to study the possible synthesis of compounds of type **17** from **1** and 2–amino–3–hydroxypyridine.



16

Condensation of **1** with 2–amino–3–hydroxypyridine in glacial acetic acid may give either of the two possible products: 6,7,14,15–tetrahydropyrido[2,1–b]pyrido[1',2':1,2]-pyrimido[4,5–g]quinazoline–4,11–dihydroxy–7,14–dione (**17**) or the benzoxazepine derivative **18**, both consistent with the empirical formula $C_{18}H_{12}N_4O_4$ (Scheme 6). However, the product obtained in this condensation is identical with the compound formed when 1,4–bis(ethoxycarbonyl)–2,5–diamino–1,4–cyclohexadiene (**19**) was allowed to react with 2–amino–3–hydroxypyridine in glacial acetic acid. The latter compound was identified as **17** on the basis of its IR spectrum which showed absorption bands at 3320 (OH), 1680 (CO) and 1640 (C=N) cm^{-1}. Similar reactions have been reported earlier.[22]

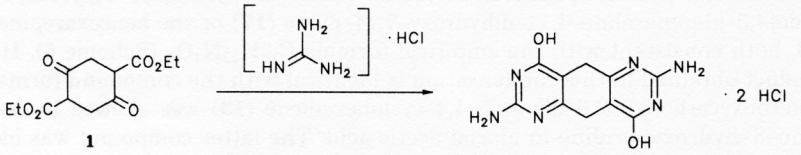
It seems that intramolecular cyclization takes place in acetic acid, and the reaction between **19**[22] or **1** and 2–amino–3–hydroxypyridine is postulated to proceed as follows:



Scheme 6.

the amino groups of **19** or the keto groups of **1** are replaced by 3–hydroxy–2–pyridylamino groups and the intermediate (**A**) form is converted to **17** by intramolecular cyclization.

The finding that aminopyrimidines inhibit the growth of microorganisms by interfering with their utilization of folic acid led to intensive search for antiinfective agents in this class of heterocyclic compounds.[10] Based on the above and in view of the reported formation of 3,8–diamino–1,6–dihydroxypyrimido[4,5–g]quinazoline (**20**),[7] diethyl 2,5–dioxocyclohexane–1,4–dicarboxylate (**1**) was treated with quanidine hydrochloride in ethanol/piperidine (Scheme 7) to give the acceptable yield of dihydrochloride **21** of quinazoline as a yellow powder. The IR spectrum of **21** showed absorption bands at 3400 (OH), 2800, 2700 (NH stretch of amine hydrochloride), 1650 (C=N), and 1540 and 1500 (NH deformation of amine hydrochloride) cm^{-1}. The mass spectrum of **21** gave (M^+–H) at *m/z* 318 corresponding to $C_{10}H_{11}N_6O_2Cl_2$.



Scheme 7.

EXPERIMENTAL

All melting points (°C) are uncorrected (Fisher electric melting point apparatus). Infrared spectra were recorded on a Unicam SP 2000 spectrophotometer from KBr pelleted sample. ^{1}H-NMR spectra (in $CDCl_3$) were recorded on Brucker 400 MHz apparatus. Mass spectra were measured on a Varian Mat 711 spectrometer, direct inlet at 70 eV. Diethyl 2,5–dioxocyclohexane–1,4–dicarboxylate (**1**) was prepared according to the method reported previously, yield 80%, m.p. 127 °C.[18]

*Condensation of **1** with 2–Aminobenzimidazole, 3–Amino–1,2,4–triazole, 5–Aminotetrazole Monohydrate, 3–Amino–1–phenyl–2–pyrazolin–5–one and 5–Amino–3–phenylpyrazole*

Method A: In polyphosphoric acid (PPA). Preparation of **2b, 4** and **6**:

A mixture of diethyl 2,5–dioxocyclohexane–1,4–dicarboxylate (**1**) (0.003 mole), the corresponding heterocyclic amine (0.006 mole) and PPA (30 g) was heated at 100 °C in water bath for 30 minutes, and then in an oil bath at 130–140 °C for 1 hour. The cooled reaction mixture was poured into ice-cold water and neutralized with 10% solution of sodium hydroxide. The precipitate obtained was collected, suspended in warm ethanol, filtered and crystallized from DMF to give compounds **2b, 4** and **6**.

Method B: In ethanol/piperidine. Preparation of **3, 5, 7, 8** and **9**:

To a mixture of **1** (0.003 mole) and the corresponding heterocyclic amine (0.006 mole) in ethanol (50 ml), piperidine (1 ml) was added. The reaction mixture was refluxed for 18 hours and left to stand for 4–5 days. The solid products that separated were filtered off and recrystallized from ethanol to give compounds **3, 5, 7, 8** and **9**.

*Cyclization of **3, 5** or **7** with Polyphosphoric Acid (PPA) to **2b, 4** and **6** Respectively:*

A mixture of **3, 5** or **7** (0.5 g) and PPA (20 g) was heated at 120–130 °C for 1 hour. The reaction mixture was left to stand for 6 hours, then poured into ice-cold water and neutralized with 10% solution of sodium hydroxide. The solid products obtained were collected, suspended in warm ethanol, filtered and crystallized from DMF to give **2b, 4** and **6**.

*The Japp-Klingemann Reaction of **1** with the Diazonium Chloride of 4–Amino Antipyrine: Formation of **10**:*

To (0.003 mole) of **1** sodium hydroxide (2,5 %; 25 ml) was added and left to stand at 0–5 °C for 24 hours. The reaction mixture was diluted with water (25 ml) and the diazonium salt of 4–aminoantipyrine (0.006 mole) was added. The pH of the medium was adjusted to 7–8 by adding 2 g of sodium bicarbonate. The solid product that separated after standing for 12 hours at 5–10 °C, was filtered and crystallized from ethanol to give **10**.

*Bis(aryl)benzo[1,2–c:,5–c']dipyrazole–3,7–diones (**12a** and **12b**):*

To a mixture of **1** (0.001 mole) and 2–pyridylhydrazine or 2–hydrazino–5–sulphobenzoic acid (0.002 mole) in ethanol (30 ml) a few drops of glacial acetic acid were added. The reaction mixture was refluxed for 6 hours and left to stand overnight. The solid product that separated in each case was filtered and recrystallized from ethanol to give **12a** or **12b**.

*Diethyl 2,5–dioxocyclohexane–1,4–dicarboxylate–2,5–bis(N,N–diphenylsulphonyl) Hydrazone (**14**):*

A mixture of **1** (0.001 mole) and *N,N*–dipohenylsulphonylhydrazide (0.0021 mole) in ethanol (30 ml) was refluxed for 6 hours, and left to stand at room temperature overnight. The precipitated solid was filtered and crystallized from ethanol to give **13**.

*2,3a,4,6,7a,8–Hexahydrobenzo[1,2–c:4,5–c']dipyrazole–3,7–dione (**14**):*

A suspension of **13** (0.5 g) in 4% alcoholic potassium hydroxide solution (40 ml) was refluxed for 1 hour, acidified with HCl (40 ml) and heated for 1 hour. The reaction mixture was left to stand overnight. The solid product that separated was filtered, recrystallized from DMF and proved to be identical with that reported in Ref.3.

*6,6a,8,14a,16–Hexahydrobenzo[1,2–b:4,5–b']bis[1,5] Substituted (Benzo)diazepine–7,15–diones (**15a–c**):*

A mixture of **1** (0.004 mole) and 4–nitro–1,2–phenylenediamine, 4–chloro–1,2–phenylenediamine or 3–methyl–1,2–phenylenediamine (0.008 mole in glacial acetic acid (30 ml) was heated at 80–90 °C for 30 minutes and filtered while hot. The solid product that separated in each case was filtered off and recrystallized from actic acid to give **15a–c**).

*6,7,14,15–Tetrahydropyrido[2,1–b]pyrido[1',2':1,2]pyrimido[4,5–quinazoline–4,11–dihydroxy–7,14–dione (**17**):*

Method A: From compound **1** and 2–amino–3–hydroxypyridine:

A mixture of **1** (0.003 mole) and 2–amino–3–hydroxypyridine (0.006 mole) in glacial acid (30 ml) was heated at 80–90 °C for 1 hour and filtered while hot. The solid product obtained after dilution with water, was collected, dried and recrystallized from acetic acid to give **17**.

Method B: From 1,4–bis(ethoxycarbonyl)–2,5–diamino–1,4–cyclohexadiene (**19**) and 2–amino–3–hydroxypyridine:

The procedure described for the preparation of **17** from **1** and 2–amino–3–hydroxypyridine was followed.

*3,5,8,10–Tetrahydro–3,8–diamino–1,6–dihydroxypyrimido[4,5–g]–quinazoline dihydrochloride (**21**):*

To a mixture of **1** (0.004 mole) and guanidine hydrochloride (0.0082 mol) in ethanol (40 ml) piperidine (1 ml) was added. The reaction mixture was refluxed for 20 hours and left to cool. The solid product that separated was filtered off, boiled with ethanol and filtered again, to give **21**.

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SAŽETAK

Sinteze nekih novih kondenziranih heterocikličkih spojeva iz 2,5–dioksocikloheksan–1,4–dikarboksilata

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U nastavku ranijih istraživanja usmjerenih prema farmakološki zanimljivim derivatima heterocikličkih spojeva sintetizirani su heterocikli **2–10, 12, 13, 15, 17** i **21**, polazeći od 2,5–dioksocikloheksan–1,4–dikarboksilata (**1**) i hidrazin, 1,2–fenilendiamin te guanidin-hidroklorida.