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6,8-Dimethylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-dione: new heterocyclizations based on S_N^H-methodology. Unexpected formation of the first iso-π-electronic analogue of the still unknown dibenzo[*a*,*o*]pycene

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Abstract—$N_{(2)}$-Oxide and 3-amino derivatives of 6,8-dimethylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-dione have been shown to react with primary alkylamines in the presence of an oxidant to produce condensed imidazolines or imidazoles. Both conversions based on S_N^H-strategy represent a new approach to imidazoline–(imidazole-)ring annulation. Heterocyclic analogues of the still unknown dibenzo[*a*,*o*]pycene were obtained as a by-products of the above transformations upon using of cyclohexylamine.

1. Introduction

Nucleophilic aromatic substitution of hydrogen (S_N^H) is usually associated with the long-known Chichibabin amination and hydroxylation of azaaromatics. Both these methods require rather drastic conditions that limit their use.[1,2] Meanwhile, modern S_N^H-procedures (e.g. oxidative amination in the liquid ammonia/potassium permanganate system[3,4]) permit not only amination of heterocycles under mild conditions but also replacement of hydrogen by O-, C-, S- and P-nucleophiles.[5] The problem, however, is that they are often suitable for inserting only one function into a molecule, since the first substituent introduced in this manner strongly deactivates the substrate to subsequent nucleophilic attack. This is a plausible reason why the use of S_N^H-reactions for the synthesis of carbo- and heterocyclic systems is rare.

Recently, we have uncovered the first aromatic substrate, namely, 6,8-dimethylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-dione (**1**), which exhibits a marvelous ability to undergo double and tandem S_N^H–S_N^H-reactions.[5–7] A remarkable property of this molecule consists in a considerable electron deficiency of the adjacent C(3) and C(4) atoms. As a consequence, compound **1** can react with bifunctional nucleophiles such as α,ω-diaminoalkanes, 1,2-diaminocycloalkanes or enamines producing polynuclear heterocycles **3**–**5** (Scheme 1).[6,7] Double oxidative amination of **1** leading to 3,4-diamino derivatives **2** is also possible but in yields not exceeding 10%.

Here, we wish to report several new S_N^H-reactions of $N_{(2)}$-oxide and 3-alkylamino derivatives of compound **1** with alkylamines and aliphatic ketone imines leading to condensed imidazolines and imidazoles as well as some other unexpected heterocyclic systems.[8]

2. Results and discussion

2.1. The interaction of 6,8-dimethylpyrimido[4,5-*c*]-pyridazine-5,7(6*H*,8*H*)-dione $N_{(2)}$-oxide and 3-alkylamino-6,8-dimethylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-diones with alkylamines

We found earlier[9] that 6,8-dimethylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-dione $N_{(2)}$-oxide (**6**) reacts with ammonia, primary or secondary amines in the presence of $KMnO_4$ or $AgPy_2MnO_4$ to give a mixture of 3-amino derivatives **7** and **8** in overall yields of 50–68% (Scheme 2). In this study we have established that similar reactions with cyclohexylamine and isopropylamine unexpectedly afford imidazolines **9a**,**b** in 4.5 and 10% yields, respectively, along with amine **8a**,**b**. The molecular structure of 3-cyclohexyl-6,8-dimethyl-7,9-dioxo-2,3,6,7,8,9-hexahydroimidazo[4′,5′;3,4]pyrimido[4,5-*c*]pyridazine-2-spirocyclohexane (**9a**) was confirmed by X-ray diffraction analysis of its perchlorate containing one methanol molecule (Fig. 1).

Keywords: 3-akylamino-6,8-dimethylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-diones; imidazoline-ring annulation; imidazole-ring annulation; pyrrole-ring annulation; nucleophilic substitution of hydrogen; dibenzo[*a*,*o*]pycene.
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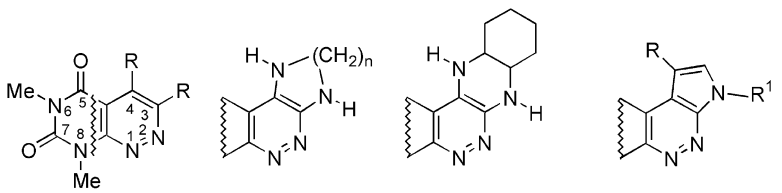
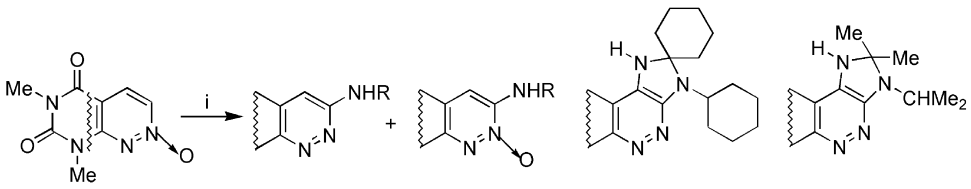


Scheme 1.



7-8 R=cyclohexyl (**a**); R=Pr^{i} (**b**); R=Pr (**c**); R=Bu (**d**); R=PhCH$_2$ (**e**); R=Et (**f**); R=cycloheptyl (**g**)

Scheme 2. (i) RNH_2, $AgPy_2MnO_4$.

The transformation of **6** into **9a** is likely to proceed via 3-cyclohexylamino derivative **7a** and has two possible pathways. The first of them (Scheme 3 (path 'a')) involves addition of **7a** across the C=N bond of cyclohexanone imine (generated in situ from cyclohexylamine) leading to *gem*-diamine **10**. Subsequent intramolecular amination and oxidation steps furnish spirocyclic product **9a**. In another pathway, compound **7a** undergoes a second amination to produce 3,4-di(cyclohexylamino) derivative **2c**, which is then oxidized and cyclized into imidazoline **9a** as shown in Scheme 3 (path 'b'). The imidazoline **9b** is evidently formed in the same manner. Both the reaction mechanisms are supported by the observation that specially prepared 3-amino derivatives **7a** and **7b** upon treatment with cyclohexylamine or isopropylamine in the presence of $AgPy_2MnO_4$ form compounds **9a** and **9b** in 60–65% yields. However, Scheme 3 (path 'a') seems to be preferable since repeated amination of compounds **7** as it was pointed out above proceeds with a low yield and only when methylamine or ethylamine are used as aminating agents.

Another question is why imidazolines **9** are formed solely from reaction of *N*-oxide **6** with cyclohexylamine and isopropylamine. We believe that it is because both of these amines have lowered oxidative potential[10] and give

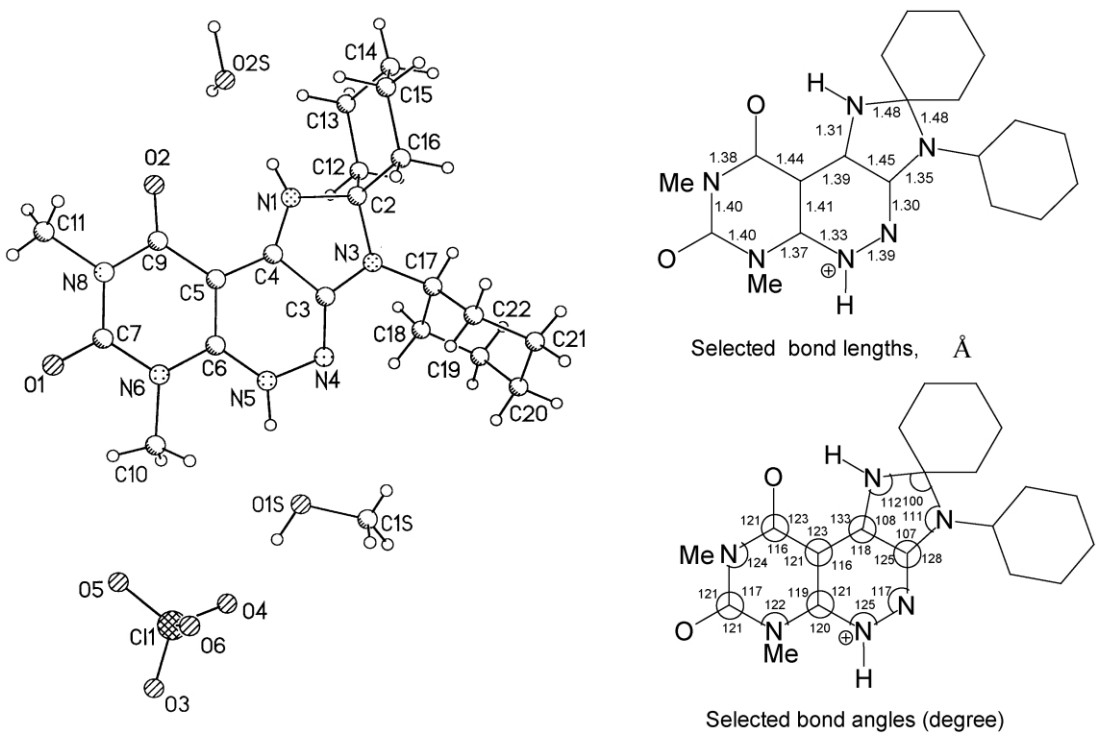
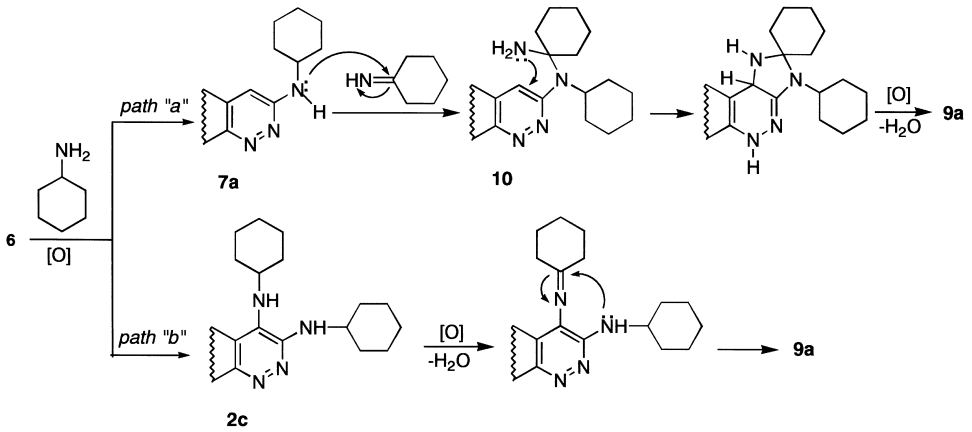


Figure 1. Molecular structure of **9a** perchlorate with crystallographic numbering scheme.



Scheme 3.

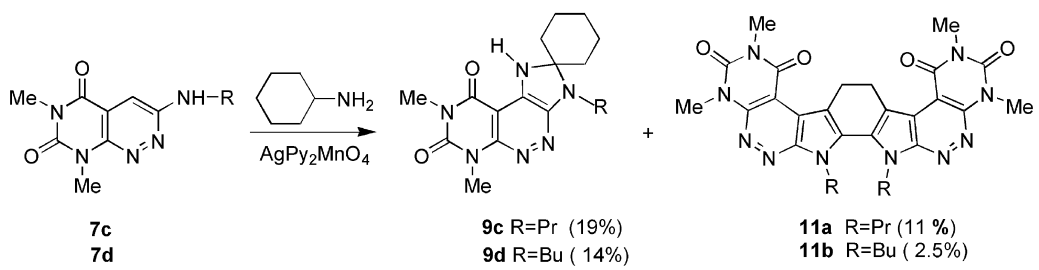
relatively stable imines. One could assume that some other alkylamines (for example, benzylamine) as well as 3-alkylamino groups of **7** can possess similar ability to oxidation. Taking this into account, we used various combinations of 3-aminopyridazines **7** and different alkylamines to prepare other fused imidazolines.

Indeed, the reaction of **7c** and **7d** with cyclohexylamine in the presence of an oxidant gives spiroimidazolines **9c** and **9d** (Scheme 4). However, in these cases, the reaction course is unexpectedly complicated by the formation of a small amount of seven-nuclear compounds **11a** and **11b** together with **9**. (The properties of **11** and the reaction mechanism are discussed in Section 2.3.). The interaction of **7a** with propylamine or butylamine affords imidazoline **13a**,**b** isomeric to **9c**,**d** and proceeds likely via imine **12** (Scheme 5).

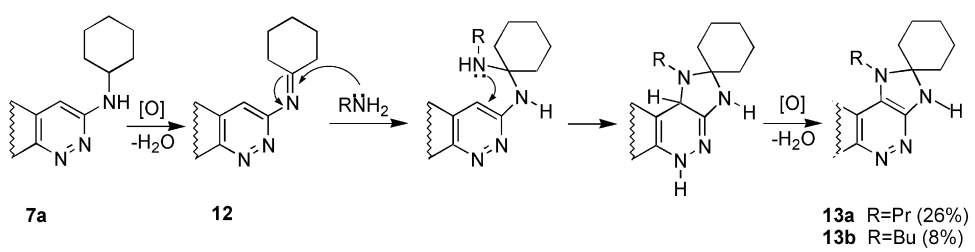
3-Benzylamino derivative **7e** reacts with alkylamines as **7a** to produce imidazoles **14a**–**d** in 18–64% yields (Scheme 6). And again, upon using, cyclohexylamine the polycycle **11c** (7.5%) was isolated as a minor product. The reaction of 3-ethylamino derivative **7f** with ethylamine/$AgPy_2MnO_4$ gave both imidazole **14e** and 3,4-di(ethylamino)-6,8-dimethylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-dione (**2b**). The **7c** and **7d** are transformed similarly into imidazoles **14f** and **14g**. It should be noted that we failed to prepare imidazole **14e** by treating **2b** with the ethylamine/oxidant mixture. This result confirms that the reaction pathway represented by Scheme 3b is not realized.

The interaction of **7c** and **7a** with benzylamine in the presence of an oxidant produces imidazoles **15a** and **15b** isomeric to **14a**,**c** (Scheme 7).

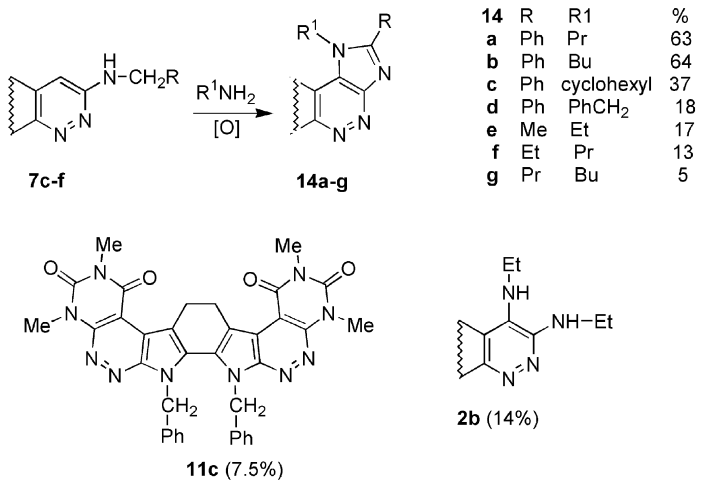
As it follows from the experimental data, the course of the above-cited reactions (briefly, 3-RNH-Het (**7**)+$R'NH_2$+[O]) depends on the relative ease of external amine and 3-RNH-group oxidation. Both benzylamine and the 3-benzylamino group possess the largest ability to oxidation and transformation into the corresponding imine (cf. **7e**→**14a**–**d**, **7c**→**15a**, **7a**→**15b**). In the absence of benzylamino groups in both reactants, the cyclohexylamino group is oxidized in the first turn and reaction proceeds via a cyclohexanone imine intermediate (cf. **7a**–**d**→**9a**–**d**, **7a**→**13a**,**b**). In those cases, when R and R^1 are not cyclohexyl, the transformation starts with the oxidation of the 3-alkylamino group (cf. **7f**→**14e**, **7c**→**14f**, **7d**→**14g**).



Scheme 4.

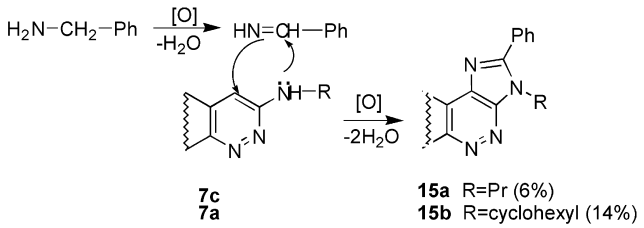


Scheme 5.



14	R	R1	%
a	Ph	Pr	63
b	Ph	Bu	64
c	Ph	cyclohexyl	37
d	Ph	$PhCH_2$	18
e	Me	Et	17
f	Et	Pr	13
g	Pr	Bu	5

Scheme 6.



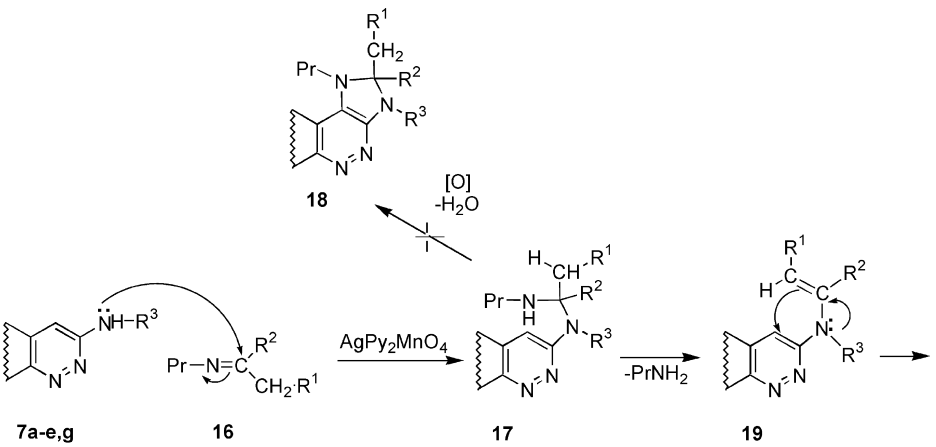
Scheme 7.

2.2. The interaction of 3-alkylamino-6,8-dimethylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-diones with ketone imines

Coming from the transformation **7→9**, we suggested that the interaction of 3-alkylamino derivatives **7** with specially prepared ketone imines might result in imidazolines **18**. However, the treatment of **7a–e,g** with *N*-propylimines **16** in the presence of an oxidant affords condensed pyrroles **20a–h** as a single product in 31–87% yields. The reason of this difference is not clear yet. Probably, intermediate *gem*-diamines **17** are not inclined to cyclization into imidazolines **18** because of their insufficient stability and steric effects. Instead, they lose a propylamine molecule yielding enamines **19**, which are transformed into pyrroles **20** in the known[7] manner (Scheme 8).

2.3. Compounds 11: properties and mechanism of formation

Compounds **11** are highly melted (mp >340°C), brightly red substances (λ_{max} 512–520 nm), rather insoluble in most



20	R^1	R^2	R^3	%
a	H	Me	Pr	87
b	- $(CH_2)_4$-		Pr	72
c	H	Me	Pr^i	81
d	H	Me	cycloheptyl	83
e	-$(CH_2)_4$-		cyclohexyl	31
f	-$(CH_2)_5$-		cycloheptyl	76
g	-$(CH_2)_4$-		Bu	56
h	-$(CH_2)_4$-		$PhCH_2$	25

Scheme 8.

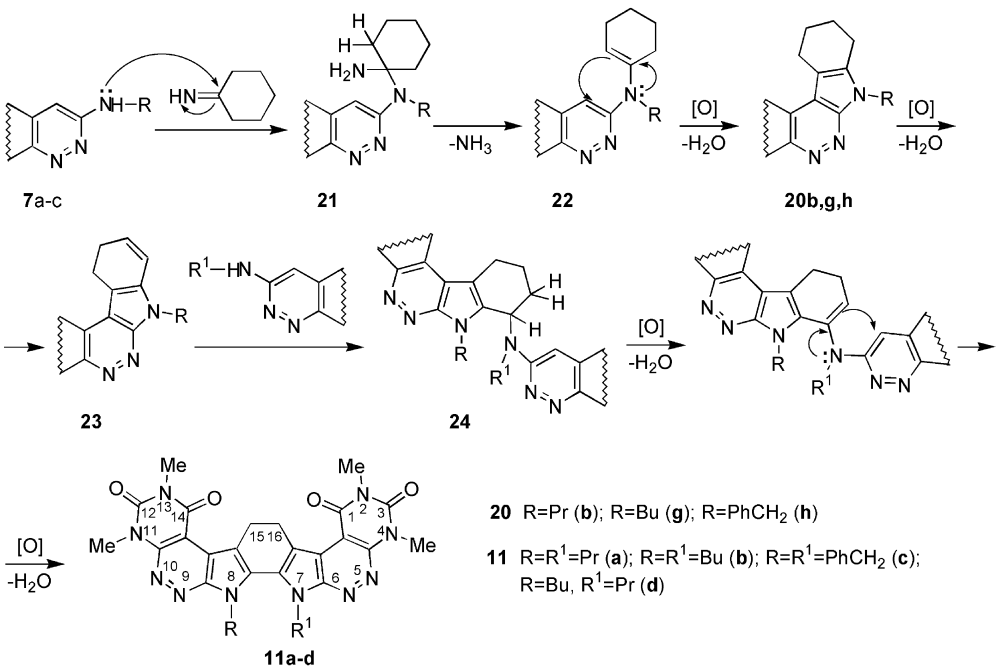
organic solvents. Their structure assignment, apart from elemental analysis, was based on the following evidence. The mass spectra of all samples show molecular ion of moderate to low intensity and a very prominent ion M−R due to loss of $N_{(7)}$-substituent. The ^{1}H NMR spectra of **11** are rather simple. They have no signals of aromatic protons but reveal singlets for two types of N−Me uracyl groups (δ 3.5 and 3.9), the set of the signals belonging to $N_{(7)}$-substituent and a characteristic singlet peak at 3.6 ppm attributed to four equivalent protons of the CH_2CH_2 chain. The latter experience a significant deshielding effect caused by proximity of $C_{(1)}$=O and $C_{(14)}$=O groups. All this testifies the existence in the molecular structure of **11** cyclohexane ring symmetrically condensed with two pyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine units at 1−2 and 3−4 bonds. In this context we would like to underline once again that compounds **11** are formed as by-products of the **7→9** and **7→14** transformations only with cyclohexylamine as the external amine. Unfortunately, we were unable to get good crystals of **11** for X-ray study and were unable to measure their ^{13}C NMR spectra because of low solubility.

Since cyclohexylamine in the presence of an oxidant forms cyclohexanone imine and 3-alkylamino derivative **7a–c** can react with imines (generated in situ or specially prepared) through two possible pathways (Schemes 3a and 8), we assumed that transformation **7a–c→11** occurs in accordance with Scheme 9 and starts from the addition of **7** across the C=N bond of cyclohexanone imine (similarly to **7→9** and **7→20**). The departure of ammonia from the resulted *gem*-diamine **21** furnishes enamine **22**, which is further cyclized into pyrrole **20** (similar to **7→20**). Subsequent oxidative step affords the key intermediate **23**, which can react with starting molecule **7** to produce adduct **24**. The subsequent oxidation and pyrrole-ring closure yield compound **11**. This mechanism is substantiated by the fact that the treatment of pyrrole **20b** with 1 equiv. of 3-propylaminopyridazine **7a** in cyclohexylamine/oxidant system results in a full conversion of the former into **11a**. Under the same conditions, pyrrole **20g** reacts with 3-propylaminopyridazine **7a** to give asymmetrically constructed **11d**. On the whole, the formation of compounds **11** looks as a cascade process[11,12] with repeating stages of oxidation, nucleophilic addition of amino groups across C=N bonds and nucleophilic substitution of the ring hydrogen atoms.

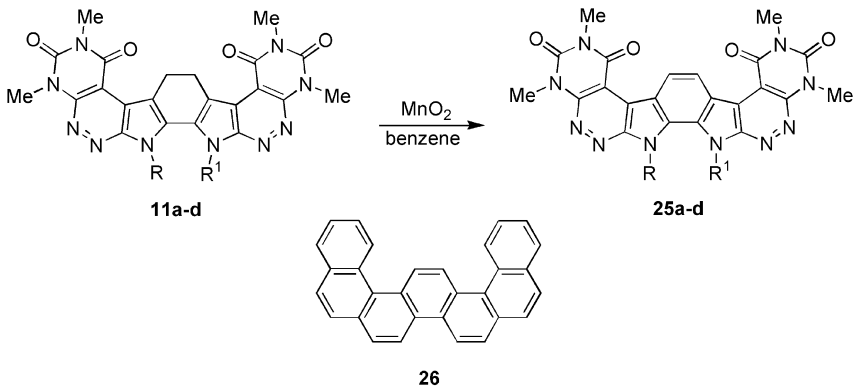
As expected, compounds **11** can be easily oxidized (e.g. by MnO_2) into derivatives of fully conjugated heterocyclic system **25** (in a trace amount they are usually present in the crude **11**). The latter represent 30π-electron analogues of yet unknown polycyclic hydrocarbon dibenzo[*a*,*o*]pycene **26** (Scheme 10). Compounds **25** have a deep red colour (λ_{max} 520−534 nm) and reveal in ^{1}H NMR spectra a downfield singlet of two aromatic protons at δ 9.6. The chloroform solutions of both polycycles **11** and **25** demonstrate yellow and dark red fluorescence with the Stokes shift equal in average 25 and 75 nm, respectively.

All the products in this study are previously unknown compounds and gave analytical and spectral data consistent with their structures.

In summary, we have developed a new method for imidazoline and imidazole ring annulation to azine nuclei based on nucleophilic substitution of hydrogen atoms. It has been also shown that 3-alkylamino-6,8-dimethylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-diones react with ketone imines to produce annulated pyrroles instead of expected imidazoles. The derivatives of new seven-membered condensed heterocyclic system—analogues of the still unknown 30π-electron arene, viz. dibenzo[*a*,*o*]-pycene **26**, have been prepared.



Scheme 9.



11, 25 R=R^1=Pr (**a**); R=R^1=Bu (**b**); R=R^1=PhCH$_2$ (**c**); R=Bu, R^1=Pr (**d**)

Scheme 10.

3. Experimental

Proton (^{1}H) nuclear magnetic resonance (NMR) spectra were recorded on a Bruker-250 (250 MHz) spectrometer with $CDCl_3$ as a solvent. Infrared (IR) spectra were recorded on a Specord IR-71 spectrometer using nujol and on a Perkin Elmer ST/IR-Spectrum 1000 spectrometer using KBr disks. Ultraviolet absorption (UV) spectra were recorded on a Specord M-40 spectrophotometer with $CHCl_3$ as a solvent. Mass spectra were measured on a MX-1321A spectrometer. Melting points were determined in glass capillaries and are uncorrected. Al_2O_3 (III–IV activity of Brockman) was used for chromatographic separations.

X-Ray structure determination. Crystallographic data for **9a**: at 110 K crystals of $C_{20}H_{29}N_6O_2{\cdot}H_2O{\cdot}MeOH$ are monoclinic, space group $P2(1)/c$, a=8.9740(19), b=10.055(2), c=27.162(6) Å, α=90°, β=90.477(4)°, γ=90°, V=2450.7(9) Å^3, Z=4, M=525.99, d_{calc}=1.426 g cm^{-3}, μ(Mo K$_\alpha$)=0.213 mm^{-1}, F(000)=1116. Intensities of 15260 reflections were measured with a SMART diffractometer at 110 K and 5997 independent reflections (R_{int}=0.0266) were used in further refinement. The structures were solved by direct method and refined by the full-matrix least squares against F^2 in the anisotropic–isotropic approximation. Hydrogen atoms were located from the Fourier synthesis and refined in the isotropic approximation. The refinement converged to $wR2$=0.1386 and GOF=1.041 for all independent reflections [R^1=0.0495 was calculated against F for observed 4460 reflections with $I>2\sigma(I)$]. All calculations were performed using SHELXTL-97 on a IBM PC AT. Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC) and allocated the deposition number CCDC 1135/114.

3.1. Synthesis of 9a and 8a from *N*-oxide 6

To a stirred solution of **6** (0.3 g, 1.5 mmol) in cyclohexylamine (20 mL), $AgPy_2MnO_4$ (0.9 g, 2.3 mmol) was added in portions at 15–20°C. After stirring a week at 20°C the liquid phase was concentrated to dryness. The residue was extracted with boiling $CHCl_3$ (50 mL). The extract was chromatographed on a column with Al_2O_3 (eluent—$CHCl_3$). The fraction with R_f 0.63 (a dark violet spot after iodine steam) gave **9a**. The following recrystallization from EtOH yielded **9a** (0.026 g, 4.5%). The fraction with R_f 0.34 (a light brown spot after iodine steam) gave **8a**. The following recrystallization from *i*-PrOH yielded **8a** (0.065 g, 22%).

3.1.1. 3-Cyclohexyl-6,8-dimethyl-7,9-dioxo-2,3,6,7,8,9-hexahydroimidazo[4′,5′;3,4]pyrimido[4,5-*c*]pyridazine-2-spirocyclohexane (9a). Compound **9a** was obtained as yellow crystals, mp >320°C (decomp.); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.20–1.90 (m, 18H, cyclohexyl), 2.66 (m, 2H, cyclohexyl), 3.06 (m, 1H, cyclohexyl), 3.34 (s, 3H, 8-Me), 3.59 (s, 3H, 6-Me), 7.59 (s, 1H, NH); IR (KBr) 1677, 1698 (C=O), 3445 cm^{-1} (N–H); UV ($CHCl_3$, λ_{max} (log ε)) 266 (4.43), 380 (3.85); MS (*m*/*z*) 384 (M$^+$). Anal. calcd for $C_{20}H_{28}N_6O_2$: C, 62.50; H, 7.29; N, 21.88. Found: C, 62.63; H, 7.15; N, 21.97.

3.1.2. 3-Cyclohexylamino-6,8-dimethylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-dione $N_{(2)}$-oxide (8a). Compound **8a** was obtained as colourless crystals, mp 242–245°C (decomp.); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.38–1.97 (m, 10H, cyclohexyl), 3.31 (m, 1H, cyclohexyl), 3.37 (s, 3H, 6-Me), 3.56 (s, 3H, 8-Me), 7.60 (s, 1H, 4-H), 9.13 (d, J=7.3 Hz, 1H, NH); IR (nujol) 1655, 1702 (C=O), 3290, 3330 cm^{-1} (N–H); UV ($CHCl_3$, λ_{max} (log ε)) 250 (4.14), 325 (3.59), 360 nm (3.42). Anal. calcd for $C_{14}H_{19}N_5O_3$: C, 55.08; H, 6.23; N, 22.95. Found: C, 54.87; H, 6.38; N, 22.83.

3.2. Synthesis of 9b and 8b from *N*-oxide 6

Synthesis of **9b** and **8b** from *N*-oxide **6** was carried out similarly.

3.2.1. 3-Isopropyl-2,2,6,8-tetramethyl-7,9-dioxo-1,2,6,7,8,9-hexahydroimidazo[4′,5′;3,4]pyrimido[4,5-*c*]pyridazine (9b). Compound **9b** was obtained as yellow crystals, R_f 0.35, mp >300°C (decomp.); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.55 (d, J=6.8 Hz, 6H, CH*Me*$_2$), 1.60 (s, 6H, C*Me*$_2$), 3.35 (s, 3H, 8-Me), 3.60 (s, 3H, 6-Me), 3.62 (m, 1H, C*H*Me$_2$), 7.17 (s, 1H, NH); IR (KBr) 1671, 1699 (C=O), 3434 cm^{-1} (N–H); UV ($CHCl_3$) λ_{max} (log ε) 266 (4.40), 379 nm (3.90); MS (*m*/*z*) 304 (M$^+$). Anal. calcd for

$C_{14}H_{20}N_6O_2$: C, 55.26; H, 6.58; N, 27.63. Found: C, 55.43; H, 6.44; N, 27.80.

3.2.2. 3-Isopropylamino-6,8-dimethylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-dione $N_{(2)}$-oxide (8b). Compound **8b** was obtained as colourless crystals, R_f 0.43, mp 225–227°C (decomp.); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.31 (d, J=6.4 Hz, 6H, $CHMe_2$), 3.38 (s, 3H, 6-Me), 3.56 (s, 3H, 8-Me), 3.62 (m, 1H, NH–*CH*), 7.60 (s, 1H, 4-H), 9.05 (m, 1H, NH); IR (nujol) 1711, 1713 (C=O), 3269 cm^{-1} (N–H); UV ($CHCl_3$, λ_{max} (log ε)) 250 (4.15), 321 (3.95), 360 nm (3.60). Anal. calcd for $C_{11}H_{15}N_5O_3$: C, 49.81; H, 5.66; N, 26.42. Found: C, 50.04; H, 5.48; N, 26.57.

3.3. General procedure for synthesis of 9a and 9b from 7a,b

To a stirred solution of **7a** (0.1 g, 0.33 mmol) in cyclohexylamine (15 mL), $AgPy_2MnO_4$ (0.3 g, 0.76 mmol) was added in portions at 15–20°C. After a week of stirring at 20°C the liquid phase was concentrated to dryness. The residue was extracted with boiling $CHCl_3$ (50 mL). The extract was chromatographed on a column with Al_2O_3 (eluent—$CHCl_3$). The following recrystallization from EtOH yielded **9a** (0.085 g, 65%) as yellow crystals.

3.3.1. Synthesis of 9c and 11a from 7c. To a stirred solution of **7c** (0.175 g, 0.7 mmol) in cyclohexylamine (15 mL), $AgPy_2MnO_4$ (0.385 g, 1 mmol) was added in portions at 15–20°C. After 3 days of stirring at 20°C the liquid phase was concentrated to dryness. The residue was extracted with boiling $CHCl_3$ (50 mL). The extract was chromatographed on a column with Al_2O_3 (eluent—$CHCl_3$–CCl_4, 13:2). The fraction with R_f 0.25 (a red spot) gave **11a**. Subsequent recrystallization from EtOH yielded **11a** (0.022 g, 11%). The fraction with R_f 0.1 (a light yellow spot) gave **9c**. Subsequent recrystallization from EtOH yielded **9c** (0.046 g, 19%).

3.3.2. 3-Propyl-6,8-dimethyl-7,9-dioxo-2,3,6,7,8,9-hexahydroimidazo[4′,5′;3,4]pyrimido[4,5-*c*]pyridazine-2-spirocyclohexane (9c). Compound **9c** was obtained as yellow crystals, mp 242–244°C (decomp.); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.94 (t, J=7.4 Hz, 3H, CH_2CH_2*Me*), 1.05–1.80 (m, 10H, cyclohexyl), 1.84 (m, 2H, CH_2*CH*$_2$Me), 3.32 (t, J=7.3 Hz, 2H, *CH*$_2$$CH_2$Me), 3.35 (s, 3H, 8-Me), 3.58 (s, 3H, 6-Me), 7.57 (s, 1H, NH); IR (nujol) 1670, 1700 (C=O), 3430 cm^{-1} (N–H); UV ($CHCl_3$) λ_{max} (log ε) 266 (4.25), 380 nm (3.63); MS (*m*/*z*) 344 (M^+). Anal. calcd for $C_{17}H_{24}N_6O_2$: C, 59.30; H, 6.98; N, 24.42. Found: C, 59.42; H, 7.01; N, 24.58.

3.3.3. 2,4,11,13-Tetramethyl-7,8-dipropyl-1,3,12,14-tetraoxo-1,2,3,4,11,1,13,14,15,16-decahydrobenzo[1,2;3,4-*a*,*a*′]di(pyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine) (11a). Compound **11a** was obtained as red crystals, mp >340°C (decomp.); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.65 (t, J=7.4 Hz, 3H, CH_2CH_2*Me*), 1.80 (m, 2H, CH_2*CH*$_2$Me), 3.55 (s, 3H, 2(13)-Me), 3.57 (s, 2H, 15(16)-CH_2), 3.98 (s, 3H, 4(11)-Me), 4.70 (t, J=7.3 Hz, 2H, *CH*$_2$$CH_2$Me)); IR (nujol) 1660, 1705 cm^{-1} (C=O); UV ($CHCl_3$) λ_{max} (log ε) 276 (4.22), 406 (4.26), 486 (4.08), 518 nm (4.13); MS (*m*/*z*) 570 (M^+). Anal. calcd for $C_{28}H_{30}N_{10}O_4$: C, 58.95; H, 5.26; N, 24.56. Found: C, 59.00; H, 5.10; N, 24.33.

3.4. Synthesis of 9d and 11b from 7d

Synthesis of **9d** and **11b** from **7d** was carried out similarly.

3.4.1. 3-Butyl-6,8-dimethyl-7,9-dioxo-2,3,6,7,8,9-hexahydroimidazo[4′,5′;3,4]pyrimido[4,5-*c*]pyridazine-2-spirocyclohexane (9d). Compound **9d** was obtained as yellow crystals, R_f 0.3, mp 183–185°C (decomp.); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.93 (t, J=7.4 Hz, 3H, $CH_2CH_2CH_2$-*Me*), 1.10–1.93 (m, 14H, cyclohexyl, CH_2*CH*$_2$*CH*$_2$Me), 3.37–3.48 (m, 2H, *CH*$_2$$CH_2CH_2$Me), 3.35 (s, 3H, 8-Me), 3.59 (s, 3H, 6-Me), 7.53 (s, 1H, NH); IR (nujol) 1633, 1700 (C=O), 3327 cm^{-1} (N–H); UV ($CHCl_3$) λ_{max} (log ε) 266 (4.18), 380 nm (3.68). Anal. calcd for $C_{18}H_{26}N_6O_2$: C, 60.34; H, 7.26; N, 23.46. Found: C, 60.35; H, 7.10; N, 23.24.

3.4.2. 2,4,11,13-Tetramethyl-7,8-dibutyl-1,3,12,14-tetraoxo-1,2,3,4,11,1,13,14,15,16-decahydrobenzo[1,2;3,4-*a*,*a*′]di(pyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine) (11b). Compound **11b** was obtained as red crystals, R_f 0.36, mp >340°C (decomp.); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.73 (t, J=7.5 Hz, 3H, $CH_2CH_2CH_2$*Me*), 0.97–1.12 (m, 2H, CH_2CH_2*CH*$_2$Me), 1.66–1.75 (m, 2H, CH_2*CH*$_2$$CH_2$Me), 3.54 (s, 3H, 2(13)-Me), 3.57 (s, 2H, 15(16)-CH_2), 3.98 (s, 3H, 4(11)-Me), 4.73 (t, J=7.3 Hz, 2H, *CH*$_2$$CH_2CH_2$Me); IR (nujol) 1673, 1713 cm^{-1} (C=O); UV ($CHCl_3$, λ_{max} (log ε) 281 (4.11), 385 (4.03), 487 (4.00), 520 nm (4.02); MS (*m*/*z*) 598 (M^+). Anal. calcd for $C_{30}H_{34}N_{10}O_4$: C, 60.20; H, 5.69; N, 23.41. Found: C, 60.09; H, 5.86; N, 23.24.

3.5. General procedure for synthesis of 13a and 13b

To a stirred solution of **7a** (0.25 g, 0.87 mmol) in propylamine (15 mL), $AgPy_2MnO_4$ (0.4 g, 1.03 mmol) was added in portions at 15–20°C. After 2 days of stirring at 20°C the liquid phase was concentrated to dryness. The residue was extracted with boiling $CHCl_3$ (50 mL). The extract was chromatographed on a column with Al_2O_3 (eluent—$CHCl_3$). Subsequent recrystallization from *i*-PrOH gave **13a** (0.076 g, 26%).

3.5.1. 1-Propyl-6,8-dimethyl-7,9-dioxo-2,3,6,7,8,9-hexahydroimidazo[4′,5′;3,4]pyrimido[4,5-*c*]pyridazine-2-spirocyclohexane (13a). Compound **13a** was obtained as yellow crystals, mp 135–137°C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.00 (t, J=7.4 Hz, 3H, CH_2CH_2*Me*), 1.17–2.14 (m, 10H, cyclohexyl and CH_2*CH*$_2$Me), 3.37 (s, 3H, 8-Me), 3.59 (m, 2H, cyclohexyl), 3.65 (s, 3H, 6-Me), 4.00 (m, 2H, *CH*$_2$$CH_2$Me), 9.26 (s, 1H, NH); IR (nujol) 1647, 1700 (C=O), 3420 cm^{-1} (N–H); UV ($CHCl_3$) λ_{max} (log ε) 267 (4.25), 391 nm (3.71); MS (*m*/*z*) 344 (M^+). Anal. calcd for $C_{17}H_{24}N_6O_2$: C, 59.30; H, 6.98; N, 24.42. Found: C, 59.50; H, 6.83; N, 24.27.

3.5.2. 1-Butyl-6,8-dimethyl-7,9-dioxo-2,3,6,7,8,9-hexahydroimidazo[4′,5′;3,4]pyrimido[4,5-*c*]pyridazine-2-spirocyclohexane (13b). Compound **13b** was obtained as yellow crystals, mp 120–122°C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.94 (t, J=7.3 Hz, 3H, $CH_2CH_2CH_2$*Me*), 1.17–1.74 (m, 10H, cyclohexyl and CH_2CH_2*CH*$_2$Me), 2.10–2.15 (m, 2H, CH_2*CH*$_2$$CH_2$Me), 3.37 (s, 3H, 8-Me), 3.61–3.67 (m, 2H, cyclohexyl), 3.65 (s, 3H, 6-Me), 3.91–4.11 (m, 2H, *CH*$_2$$CH_2CH_2$Me), 9.25 (s, 1H, NH); IR (nujol) 1633, 1687

(C═O), 3353 cm^{-1} (N–H); UV ($CHCl_3$) λ_{max} (log ε) 267 (4.25), 390 nm (3.71); MS (*m/z*) 358 (M^+). Anal. calcd for $C_{18}H_{26}N_6O_2$: C, 60.34; H, 7.26; N, 23.46. Found: C, 60.51; H, 7.24; N, 23.50.

3.6. General procedure for synthesis of 14a,b,d

To a stirred solution of **7e** (0.2 g, 0.67 mmol) in propylamine (18 mL), $AgPy_2MnO_4$ (0.385 g, 1 mmol) was added in portions at 15–20°C. After 2 days of stirring at 20°C the liquid phase was concentrated to dryness. The residue was extracted with boiling $CHCl_3$ (50 mL). The extract was chromatographed on a column with Al_2O_3 (eluent—$CHCl_3$). The following recrystallization from *i*-PrOH gave **14a** (0.148 g, 63%).

3.6.1. 1-Propyl-2-phenyl-6,8-dimethylimidazo[4′,5′;3,4]pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (14a). Compound **14a** was obtained as colourless crystals, mp 237–239°C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.64 (t, *J*=7.4 Hz, 3H, CH_2CH_2*Me*), 1.60 (m, 2H, CH_2*CH*$_2$Me), 3.50 (s, 3H, 8-Me), 4.00 (s, 3H, 6-Me), 4.90 (t, *J*=7.3 Hz, 2H, *CH*$_2$$CH_2$Me), 7.57–7.78 (m, 5H, Ph); IR (nujol) 1675, 1705 cm^{-1} (C═O); UV ($CHCl_3$) λ_{max} (log ε) 250 (4.40), 310 (3.85), 357 nm (3.82). Anal. calcd for $C_{18}H_{18}N_6O_2$: C, 61.71; H, 5.14; N, 24.00. Found: C, 61.54; H, 5.27; N, 24.17.

3.6.2. 1-Butyl-2-phenyl-6,8-dimethylimidazo[4′,5′;3,4]pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (14b). Compound **14b** was obtained as colourless crystals, mp 177–180°C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.67 (t, *J*=7.3 Hz, 3H, $(CH_2)_2CH_2$*Me*), 0.95–1.10 (m, 2H, $(CH_2)_2$*CH*$_2$Me), 1.40–1.55 (m, 2H, CH_2*CH*$_2$$CH_2$Me), 3.53 (s, 3H, 8-Me), 3.99 (s, 3H, 6-Me), 4.95 (t, *J*=7.4 Hz, 2H, *CH*$_2$$(CH_2)_2$Me), 7.53–7.78 (m, 5H, Ph); IR (nujol) 1700, 1713 cm^{-1} (C═O); UV ($CHCl_3$) λ_{max} (log ε) 250 (4.46), 311 (3.92), 357 nm (3.89). Anal. calcd for $C_{19}H_{20}N_6O_2$: C, 62.64; H, 5.49; N, 23.08. Found: C, 62.83; H, 5.58; N, 23.16.

3.6.3. 1-Benzyl-2-phenyl-6,8-dimethylimidazo[4′,5′;3,4]pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (14d). Compound **14d** was obtained as colourless crystals, mp 198–200°C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 3.43 (s, 3H, 8-Me), 3.97 (s, 3H, 6-Me), 6.23 (s, 2H, *CH*$_2$Ph), 6.71–7.20 (m, 5H, CH_2*Ph*), 7.49–7.75 (m, 5H, Ph); IR (nujol) 1670, 1703 cm^{-1} (C═O); UV ($CHCl_3$) λ_{max} (log ε) 251 (4.43), 308 (3.81), 358 nm (3.85). Anal. calcd for $C_{22}H_{18}N_6O_2$: C, 66.33; H, 4.52; N, 21.11. Found: C, 66.60; H, 4.45; N, 21.23.

3.7. Synthesis of 14c and 11c from 7e

To a stirred solution of **7e** (0.164 g, 0.56 mmol) in cyclohexylamine (15 mL), $AgPy_2MnO_4$ (0.385 g, 1 mmol) was added in portions at 15–20°C. After 2 days of stirring at 20°C the liquid phase was concentrated to dryness. The residue was extracted with boiling $CHCl_3$ (50 mL). The extract was chromatographed on a column with Al_2O_3 (eluent—$CHCl_3$–CCl_4, 13:2). The fraction with R_f 0.36 (a red spot) gave **11c**. Subsequent recrystallization from EtOH yielded **11c** (0.014 g, 7.5%). The fraction with R_f 0.2 gave **14c**. Subsequent recrystallization from EtOH yielded **14c** (0.08 g, 37%).

3.7.1. 1-Cyclohexyl-2-phenyl-6,8-dimethylimidazo[4′,5′;3,4]pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (14c). Compound **14c** was obtained as colourless crystals, mp 279–281°C (decomp.); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.80–2.00 (m, 10H, cyclohexyl), 3.54 (s, 3H, 8-Me), 3.99 (s, 3H, 6-Me), 5.45 (m, 1H, cyclohexyl), 7.48–7.68 (m, 5H, Ph); IR (nujol) 1670, 1700 cm^{-1} (C═O); UV ($CHCl_3$) λ_{max} (log ε) 250 (4.48), 310 (3.88), 355 nm (3.81); MS (*m/z*) 390 (M^+). Anal. calcd for $C_{21}H_{22}N_6O_2$: C, 64.62; H, 5.64; N, 21.54. Found: C, 64.85; H, 5.45; N, 21.32.

3.7.2. 2,4,11,13-Tetramethyl-7,8-dibenzyl-1,3,12,14-tetraoxo-1,2,3,4,11,1,13,14,15,16-decahydrobenzo-[1,2;3,4-*a*,*a*′]di(pyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine) (11c). Compound **11c** was obtained as red crystals, R_f 0.15, mp >340°C (decomp.); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 3.53 (s, 3H, 2(13)-Me), 3.56 (s, 2H, 15(16)-CH_2), 3.94 (s, 3H, 4(11)-Me), 5.90 (s, 2H, *CH*$_2$Ph), 6.86 (m, 2H, Ph), 7.10 (m, 3H, Ph); IR (nujol) 1650, 1705 cm^{-1} (C═O); UV ($CHCl_3$, λ_{max} (log ε) 402 (4.23), 481 (4.25), 512 nm (4.26); MS (*m/z*) 666 (M^+). Anal. calcd for $C_{36}H_{30}N_{10}O_4$: C, 64.86; H, 4.50; N, 21.20. Found: C, 64.97; H, 4.32; N, 21.21.

3.8. Synthesis of 14e and 2b from 7f

To a stirred solution of **7f** (0.1 g, 0.43 mmol) in ethylamine (30 mL), $AgPy_2MnO_4$ (0.171 g, 0.45 mmol) was added in portions at 15–20°C. After 2 days of stirring at 20°C the liquid phase was concentrated to dryness. The residue was extracted with boiling $CHCl_3$ (50 mL). The extract was chromatographed on a column with Al_2O_3 (eluent—$CHCl_3$–CCl_4, 10:1). The fraction with R_f 0.70 (a yellow spot) gave **2b**. Subsequent recrystallization from *i*-PrOH yielded **2b** (0.017 g, 14%). The fraction with R_f 0.4 gave **14e**. Subsequent recrystallization from EtOH yielded **14e** (0.02 g, 17%).

3.8.1. 1-Ethyl-2,6,8-trimethylimidazo[4′,5′;3,4] pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (14e). Compound **14e** was obtained as colourless crystals, mp 191–192°C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.42 (t, *J*=7.1 Hz, 3H, CH_2*Me*), 2.77 (s, 3H, 2-Me), 3.52 (s, 3H, 8-Me), 3.97 (s, 3H, 6-Me), 4.89 (q, 2H, *CH*$_2$Me); IR (nujol) 1680, 1710 cm^{-1} (C═O). Anal. calcd for $C_{12}H_{14}N_6O_2$: C, 52.55; H, 5.11; N, 30.66. Found: C, 52.34; H, 5.09; N, 30.76.

3.8.2. 3,4-Di(ethylamino)-6,8-dimethylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-dione (2b). Compound **2b** was obtained as yellow crystals, mp 134–135°C; ^{1}H NMR (DMSO-D_6, 250 MHz) δ 1.17 (t, *J*=7.14 Hz, 3H, CH_2*Me*), 1.19 (t, *J*=7.14 Hz, 3H, CH_2*Me*), 3.20 (s, 3H, 6-Me), 3.33 (m, 2H, *CH*$_2$Me), 3.45 (s, 3H, 8-Me), 3.70 (m, 2H, *CH*$_2$Me), 5.77 (m, 1H, 3-NH), 9.04 (m, 1H, 4-NH); IR (nujol) 1655, 1715 (C═O), 3245, 3375 cm^{-1} (N–H). Anal. calcd for $C_{12}H_{18}N_6O_2$: C, 51.80; H, 6.47; N, 30.21. Found: C, 51.64; H, 6.48; N, 30.52.

3.9. Synthesis of 14f and 14g from 7c,d

Synthesis of **14f** and **14g** from **7c**,**d** was carried out similarly.

3.9.1. 1-Propyl-2-ethyl-6,8-trimethylimidazo[4′,5′;3,4]pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (14f). Compound **14f** was obtained as colourless crystals,

mp 272–275°C (decomp.); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.07 (t, J=7.4 Hz, 3H, CH_2CH_2*Me*), 1.32 (t, J=7.4 Hz, 3H, CH_2*Me*), 1.85 (m, 2H, CH_2*CH*$_2$Me), 3.54 (s, 3H, 8-Me), 4.00 (s, 3H, 6-Me), 4.09 (m, 2H, *CH*$_2$Me), 4.83–5.10 (m, 2H, *CH*$_2$CH$_2$Me); IR (nujol) 1660, 1700 cm^{-1} (C=O). Anal. calcd for $C_{14}H_{18}N_6O_2$: C, 55.63; H, 5.96; N, 27.82. Found: C, 55.49; H, 5.72; N, 27.65.

3.9.2. 1-Butyl-2-propyl-6,8-trimethylimidazo [4′,5′;3,4]pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (14g). Compound **14g** was obtained as colourless crystals, mp 290–293°C (decomp.); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.69 (t, J=7.3 Hz, 3H, $CH_2CH_2CH_2$*Me*), 1.00 (t, J=7.2 Hz, 3H, CH_2CH_2*Me*), 1.46–2.03 (m, 6H, CH_2*CH*$_2$*CH*$_2$Me and CH_2*CH*$_2$Me), 3.54 (s, 3H, 8-Me), 3.86 (m, 2H, *CH*$_2$CH$_2$Me), 4.00 (s, 3H, 6-Me), 4.97–5.07 (m, 2H, *CH*$_2$CH$_2$CH$_2$Me); IR (nujol) 1687, 1727 cm^{-1} (C=O). Anal. calcd for $C_{16}H_{22}N_6O_2$: C, 58.18; H, 6.67; N, 25.46. Found: C, 58.30; H, 6.57; N, 25.27.

3.10. General procedure for synthesis of 15a,b

To a stirred solution of **7c** (0.145 g, 0.58 mmol) in benzylamine (18 mL), $AgPy_2MnO_4$ (0.3 g, 0.78 mmol) was added in portions at 15–20°C. After a week of stirring at 20°C the liquid phase was concentrated to dryness. The residue was extracted with boiling $CHCl_3$ (50 mL). The extract was chromatographed on a column with Al_2O_3 (eluent—$CHCl_3$–CCl_4, 10:1). The following recrystallization from *i*-PrOH gave **15a** (0.012 g, 6%).

3.10.1. 3-Propyl-2-phenyl-6,8-dimethylimidazo [5′,4′;3,4]pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (15a). Compound **15a** was obtained as fawn-coloured crystals, mp 221–223°C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.91 (t, J=7.4 Hz, 3H, CH_2CH_2*Me*), 1.95–2.04 (m, 2H, CH_2*CH*$_2$Me), 3.54 (s, 3H, 8-Me), 3.96 (s, 3H, 6-Me), 4.54 (t, J=7.6 Hz, 2H, *CH*$_2$CH$_2$Me), 7.58–7.93 (m, 5H, Ph); IR (nujol) 1673, 1713 cm^{-1} (C=O); UV ($CHCl_3$) λ_{max} (log ε) 320 (4.40), 357 (3.90), 378 nm (3.71). Anal. calcd for $C_{18}H_{18}N_6O_2$: C, 61.71; H, 5.14; N, 24.00. Found: C, 61.83; H, 5.08; N, 24.23.

3.10.2. 3-Cyclohexyl-2-phenyl-6,8-dimethylimidazo [5′,4′;3,4]pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (15b). Compound **15b** was obtained as fawn-coloured crystals, mp 275–276°C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.29–2.93 (m, 10H, cyclohexyl), 3.52 (s, 3H, 8-Me), 3.95 (s, 3H, 6-Me), 4.51 (m, 1H, cyclohexyl), 7.24–7.79 (m, 5H, Ph); IR (nujol) 1653, 1700 cm^{-1} (C=O); UV ($CHCl_3$) λ_{max} (log ε) 319 (4.19), 357 (3.87), 378 nm (3.70); MS (*m*/*z*) 390 (M^+). Anal. calcd for $C_{21}H_{22}N_6O_2$: C, 64.62; H, 5.64; N, 21.54. Found: C, 64.53; H, 5.72; N, 21.46.

3.11. General procedure for synthesis of 20a–h

To a stirred solution of **7** (1 mmol) in *N*-alkylketone imine (10 mL), $AgPy_2MnO_4$ (0.158 g, 1 mmol) was added in portions at 15–20°C. After 3 days of stirring at 20°C the liquid phase was concentrated to dryness. The residue was extracted with boiling $CHCl_3$ (50 mL). The extract was chromatographed on a column with Al_2O_3 (eluent—$CHCl_3$). The following recrystallization from *i*-PrOH gave 25–87% **20**.

3.11.1. 3-Propyl-2,6,8-trimethylpyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (20a). Compound **20a** was obtained as bright yellow crystals, mp 205–206°C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.95 (t, J=7.4 Hz, 3H, CH_2CH_2*Me*), 1.88 (m, 2H, CH_2*CH*$_2$Me), 2.59 (s, 3H, 2-Me), 3.50 (s, 3H, 8-Me), 3.90 (s, 3H, 6-Me), 4.37 (t, J=7.4 Hz, 2H, *CH*$_2$CH$_2$Me), 6.97 (s, 1H, 1-H); IR (KBr) 1657, 1698 (C=O), 2964 cm^{-1} (C–H); UV ($CHCl_3$) λ_{max} (log ε) 331 (3.94), 394 nm (3.78). Anal. calcd for $C_{14}H_{17}N_5O_2$: C, 58.54; H, 5.92; N, 24.39. Found: C, 58.37; H, 6.10; N, 24.53.

3.11.2. 6,8-Dimethyl-3-propyl-1,2-tetramethylenepyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (20b). Compound **20b** was obtained as bright yellow crystals, mp 146–147°C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.94 (t, J=7.3 Hz, 3H, CH_2CH_2*Me*), 1.85 (m, 2H, CH_2*CH*$_2$Me), 1.93 (m, 4H, CH_2(*CH*$_2$)$_2$CH$_2$), 2.85 (t, J=6.3 Hz, 2H, *CH*$_2$(CH$_2$)$_2$CH$_2$), 3.28 (t, J=6.3 Hz, 2H, CH_2(CH$_2$)$_2$*CH*$_2$), 3.48 (s, 3H, 8-Me), 3.90 (s, 3H, 6-Me), 4.30 (t, J=7.3 Hz, 2H, *CH*$_2$CH$_2$Me); IR (KBr) 1660, 1707 cm^{-1} (C=O). Anal. calcd for $C_{17}H_{21}N_5O_2$: C, 62.39; H, 6.42; N, 21.41. Found: C, 62.58; H, 6.61; N, 21.57.

3.11.3. 3-Isopropyl-2,6,8-trimethylpyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (20c). Compound **20c** was obtained as bright yellow crystals, mp 207–208°C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.75 (d, J=6.9 Hz, 6H, CH*Me*$_2$), 2.66 (s, 3H, 2-Me), 3.50 (s, 3H, 8-Me), 3.90 (s, 3H, 6-Me), 4.97 (m, J=6.9 Hz, 1H, *CH*Me$_2$), 7.06 (s, 1H, 1-H); IR (KBr) 1663, 1696 (C=O), 2929 cm^{-1} (C–H). Anal. calcd for $C_{14}H_{17}N_5O_2$: C, 58.54; H, 5.92; N, 24.39. Found: C, 58.48; H, 5.73; N, 24.61.

3.11.4. 3-Cycloheptyl-2,6,8-trimethylpyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (20d). Compound **20d** was obtained as bright yellow crystals, mp 258–259°C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.64–1.78 (m, 4H, cycloheptyl), 1.88–1.98 (m, 6H, cycloheptyl), 2.55–2.65 (m, 2H, cycloheptyl), 2.61 (s, 3H, 2-Me), 3.50 (s, 3H, 8-Me), 3.91 (s, 3H, 6-Me), 4.70 (m, 1H, cycloheptyl); 6.95 (s, 1H, 1-H); IR (KBr) 1661, 1707 (C=O), 2927 cm^{-1} (C–H); UV ($CHCl_3$) λ_{max} (log ε) 330 (3.94), 398 nm (3.80). Anal. calcd for $C_{18}H_{23}N_5O_2$: C, 63.34; H, 6.74; N, 20.53. Found: C, 63.21; H, 6.61; N, 20.70.

3.11.5. 3-Cyclohexyl-6,8-dimethyl-1,2-tetramethylenepyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (20e). Compound **20e** was obtained as bright yellow crystals, mp 222–225°C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.35–1.50 (m, 2H, cyclohexyl), 1.67–1.93 (m, 10H, cyclohexyl and CH_2*CH*$_2$CH$_2$CH$_2$), 2.57–2.66 (m, 2H, CH$_2$CH$_2$*CH*$_2$CH$_2$), 2.88 (m, 2H, *CH*$_2$(CH$_2$)$_2$CH$_2$), 3.29 (m, 2H, CH$_2$(CH$_2$)$_2$*CH*$_2$), 3.49 (s, 3H, 8-Me), 3.94 (s, 3H, 6-Me), 4.40 (m, 1H, cyclohexyl); IR (nujol) 1660, 1727 cm^{-1} (C=O); UV ($CHCl_3$) λ_{max} (log ε) 258 (4.27), 337 (3.87), 424 nm (3.72). Anal. calcd for $C_{20}H_{25}N_5O_2$: C, 65.40; H, 6.81; N, 19.07. Found: C, 65.29; H, 6.58; N, 18.95.

3.11.6. 3-Cycloheptyl-6,8-dimethyl-1,2-pentamethylenepyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (20f). Compound **20f** was obtained as bright yellow crystals, mp 211–212°C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ

1.60–2.00 (m, 18H, cycloheptyl and $CH_2(CH_2)_3CH_2$), 3.07 (m, 2H, $CH_2(CH_2)_3CH_2$), 3.50 (s, 3H, 8-Me), 3.56 (m, 2H, $CH_2(CH_2)_3CH_2$), 4.01 (s, 3H, 6-Me), 5.70 (m, 1H, cycloheptyl); IR (KBr) 1654, 1705 cm^{-1} (C=O); UV ($CHCl_3$) λ_{max} (log ε) 340 (3.94), 427 nm (3.79). Anal. calcd for $C_{21}H_{27}N_5O_2$: C, 66.14; H, 7.09; N, 18.37. Found: C, 66.00; H, 7.32; N, 18.54.

3.11.7. 3-Butyl-6,8-dimethyl-1,2-tetramethylenepyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (20g). Compound **20g** was obtained as bright yellow crystals, mp 143–145°C; ^1H NMR ($CDCl_3$, 250 MHz) δ 0.93 (t, J=7.3 Hz, 3H, $CH_2CH_2CH_2Me$), 1.39 (m, 2H, $CH_2CH_2CH_2Me$), 1.84 (m, 6H, $CH_2(CH_2)_2CH_2$ and CH_2-CH_2CH_2Me), 2.85 (t, J=6.3 Hz, 2H, $CH_2(CH_2)_2CH_2$), 3.31 (t, J=6.3 Hz, 2H, $CH_2(CH_2)_2CH_2$), 3.49 (s, 3H, 8-Me), 3.90 (s, 3H, 6-Me), 4.34 (t, J=7.3 Hz, 2H, $CH_2CH_2CH_2Me$); IR (KBr) 1667, 1700 cm^{-1} (C=O); UV ($CHCl_3$) λ_{max} (log ε) 337 (3.89), 348 (3.86), 422 nm (3.70). Anal. calcd for $C_{18}H_{23}N_5O_2$: C, 63.34; H, 6.74; N, 20.53. Found: C, 63.22; H, 6.57; N, 20.71.

3.11.8. 3-Benzyl-6,8-dimethyl-1,2-tetramethylenepyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine-7,9(6*H*,8*H*)-dione (20h). Compound **20h** was obtained as bright yellow crystals, mp 193–195°C; ^1H NMR ($CDCl_3$, 250 MHz) δ 1.85 (m, 4H, $CH_2(CH_2)_2CH_2$), 2.75 (t, J=6.3 Hz, 2H, $CH_2(CH_2)_2CH_2$), 3.29 (t, J=6.3 Hz, 2H, $CH_2(CH_2)_2CH_2$), 3.50 (s, 3H, 8-Me), 3.92 (s, 3H, 6-Me), 5.60 (s, 2H, CH_2Ph), 7.13–7.30 (m, 5H, CH_2Ph); IR (KBr) 1660, 1700 cm^{-1} (C=O). UV ($CHCl_3$) λ_{max} (log ε) 336 (3.77), 347 (3.73), 416 nm (3.62). Anal. calcd for $C_{21}H_{21}N_5O_2$: C, 67.20; H, 5.60; N, 18.67. Found: C, 67.37; H, 5.43; N, 18.81.

3.12. General procedure for synthesis of 11a,d from 20b,g and 7a

To a stirred solution of **20b** (0.083 g, 0.25 mmol) and $AgPy_2MnO_4$ (0.23 g, 0.6 mmol) in cyclohexylamine (15 mL), solution of **7a** (0.064 g, 0.25 mmol) in cyclohexylamine (15 mL) was added at 15–20°C. After 5 days of stirring at 20°C the liquid phase was concentrated to dryness. The residue was extracted with boiling $CHCl_3$ (50 mL). The extract was chromatographed on a column with Al_2O_3 (eluent—$CHCl_3$–CCl_4, 6:1). Subsequent recrystallization from EtOH yielded **11a** (0.074 g, 52%).

3.12.1. 2,4,11,13-Tetramethyl-7-propyl-8-butyl-1,3,12,14-tetraoxo-1,2,3,4,11,1,13,14,15,16-decahydrobenzo[1,2;3,4-*a*,*a*′]di(pyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine) (11d). Compound **11d** was obtained as red crystals in 49% yield, R_f 0.31, mp >340°C (decomp.); ^1H NMR ($CDCl_3$, 250 MHz) δ 0.65 (t, J=7.5 Hz, 3H, CH_2-CH_2CH_2Me), 0.73 (t, J=7.2 Hz, 3H, CH_2CH_2Me), 1.14 (m, 2H, $CH_2CH_2CH_2Me$), 1.80 (m, 4H, CH_2CH_2Me and $CH_2CH_2CH_2Me$), 3.54 (pseudosinglet, 6H, 2(13)-Me), 3.57 (pseudosinglet, 4H, 15(16)-CH_2), 3.97 (pseudosinglet, 6H, 4(11)-Me), 4.70 (t, J=7.3 Hz, 2H, CH_2CH_2Me), 4.74 (t, J=7.3 Hz, 2H, $CH_2CH_2CH_2Me$); IR (nujol) 1665, 1710 cm^{-1} (C=O); UV ($CHCl_3$, λ_{max} (log ε) 278 (4.15), 398 (4.02), 486 (3.90), 519 nm (3.98); MS (m/z) 584 (M^+). Anal. calcd for $C_{29}H_{32}N_{10}O_4$: C, 59.59; H, 5.48; N, 23.97. Found: C, 59.71; H, 5.33; N, 23.89.

3.13. General procedure for synthesis of 25a–d from 11a–d

A stirred suspension of **11b** (0.020 g, 0.033 mmol) and MnO_2 (0.0052 g, 0.06 mmol) in benzene (30 mL) was refluxed. After a week of refluxing, reaction mixture was concentrated to dryness. The residue was extracted with boiling $CHCl_3$ (50 mL). The extract was chromatographed on a column with Al_2O_3 (1×5 cm) (eluent—$CHCl_3$). 0.019 g (97%) red crystals of **25b** were obtained.

3.13.1. 2,4,11,13-Tetramethyl-7,8-dipropyl-1,3,12,14-tetraoxo-1,2,3,4,11,12,13,14-octahydrobenzo[1,2;3,4-*a*,*a*′]di(pyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine) (25a). Compound **25a** was obtained as red crystals in 95% yield, mp >340°C (decomp.); ^1H NMR ($CDCl_3$, 250 MHz) δ 0.73 (t, J=7.4 Hz, 3H, CH_2CH_2Me), 1.92 (m, 2H, CH_2CH_2Me), 3.64 (s, 3H, 2(13)-Me), 4.04 (s, 3H, 4(11)-Me), 4.99 (t, J=7.3 Hz, 2H, CH_2CH_2Me), 9.58 (s, 1H, 15(16)-H); IR (nujol) 1653, 1706 cm^{-1} (C=O); UV ($CHCl_3$) λ_{max} (log ε) 281 (4.45), 384 (4.30), 404 sh (4.26), 534 nm (3.35). Anal. calcd for $C_{28}H_{28}N_{10}O_4$: C, 59.15; H, 4.93; N, 24.65. Found: C, 58.96; H, 5.12; N, 24.51.

3.13.2. 2,4,11,13-Tetramethyl-7,8-dibutyl-1,3,12,14-tetraoxo-1,2,3,4,11,12,13,14-octahydrobenzo[1,2;3,4-*a*,*a*′]di(pyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine) (25b). Compound **25b** was obtained as red crystals, mp >340°C (decomp.); ^1H NMR ($CDCl_3$, 250 MHz) δ 0.78 (t, J=7.3 Hz, 3H, $CH_2CH_2CH_2Me$), 1.11 (m, 2H, CH_2CH_2-CH_2Me), 1.81 (m, 2H, $CH_2CH_2CH_2Me$), 3.64 (s, 3H, 2(13)-Me), 4.04 (s, 3H, 4(11)-Me), 5.04 (t, J=7.5 Hz, 2H, $CH_2CH_2CH_2Me$), 9.57 (s, 1H, 15(16)-H); IR (nujol) 1660, 1713 cm^{-1} (C=O); UV ($CHCl_3$, λ_{max} (log ε) 281 (4.54), 384 (4.40), 527 nm (3.54). Anal. calcd for $C_{30}H_{32}N_{10}O_4$: C, 60.40; H, 5.37; N, 23.49. Found: C, 60.52; H, 5.25; N, 23.58.

3.13.3. 2,4,11,13-Tetramethyl-7,8-dibenzyl-1,3,12,14-tetraoxo-1,2,3,4,11,12,13,14-octahydrobenzo[1,2;3,4-*a*,*a*′]di(pyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine) (25c). Compound **25c** was obtained as red crystals in 93% yield, mp >340°C (decomp.); ^1H NMR ($CDCl_3$, 250 MHz) δ 3.62 (s, 3H, 2(13)-Me), 3.95 (s, 3H, 4(11)-Me), 5.96 (s, 2H, CH_2Ph), 6.87 (m, 2H, Ph), 7.19 (m, 3H, Ph), 9.60 (s, 1H, 15(16)-H); IR (nujol) 1667, 1713 cm^{-1} (C=O); UV ($CHCl_3$, λ_{max} (log ε) 279 (4.58), 384 (4.19), 530 nm (3.52). Anal. calcd for $C_{36}H_{28}N_{10}O_4$: C, 65.06; H, 4.22; N, 21.08. Found: C, 64.89; H, 4.03; N, 21.26.

3.13.4. 2,4,11,13-Tetramethyl-7-propyl-8-butyl-1,3,12,14-tetraoxo-1,2,3,4,11,12,13,14-octahydrobenzo[1,2;3,4-*a*,*a*′]di(pyrrolo[2′,3′;3,4]pyrimido[4,5-*c*]pyridazine) (25d). Compound **25d** was obtained as red crystals in 95% yield, mp >340°C (decomp.); ^1H NMR ($CDCl_3$, 250 MHz) δ 0.75 (t, J=7.5 Hz, 3H, $CH_2CH_2CH_2Me$), 0.78 (t, J=7.0 Hz, 3H, CH_2CH_2Me), 1.09 (m, 2H, $CH_2CH_2CH_2Me$), 1.84 (m, 4H, CH_2CH_2Me and $CH_2CH_2CH_2Me$), 3.65 (pseudosinglet, 6H, 2(13)-Me), 4.04 (pseudosinglet, 6H, 4(11)-Me), 4.99 (t, J=7.3 Hz, 2H, CH_2CH_2Me), 5.02 (t, J=7.5 Hz, 2H, $CH_2CH_2CH_2Me$), 9.57 (pseudosinglet, 2H, 15(16)-H); IR (nujol) 1658, 1710 cm^{-1} (C=O); UV ($CHCl_3$, λ_{max} (log ε) 282 (4.61), 386 (4.47), 486

(3.90), 520 (3.48). Anal. calcd for $C_{29}H_{30}N_{10}O_4$: C, 59.79; H, 5.15; N, 24.05. Found: C, 59.93; H, 5.01; N, 23.88.

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