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Transformations of (1*E*,3*E*)-1-(benzoylamino)-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylates into pyridine and pyrrole derivatives

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ABSTRACT

New, highly functionalised (1*E*,3*E*)-1-(benzoylamino)-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylates proved to be useful and versatile reagents in the formation of highly substituted pyridine, *N*-aminopyridine, pyrrole and pyrido[3,4-*c*]pyridazine derivatives. The formation of the particular type heterocyclic system is dependent on the starting (1*E*,3*E*)-1-(benzoylamino)-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylate. By an appropriate choice of different ester groups it is possible to drive the reactions towards the formation of either pyridine or pyrrole derivatives.

1. Introduction

Pyridines and pyrroles are basic structural elements of many important metabolites. Among others, pyridine is an integral part of niacin, while pyrrole is irreversibly connected with haem and chlorophyll. Many synthetic routes have been developed for the synthesis of pyridines and pyrroles.[1a–g] However, literature concerning highly functionalised ring systems, especially those possessing additional ester and amino groups, is scarce. A widely recognised way of producing highly substituted pyridines and pyridinones is by the cycloaddition of acetylenes or olefins to 2(1*H*)-pyrazinones.[2a–d] On the other hand, to obtain highly substituted pyrrole derivatives, a few different approaches have been used.[3a–e] Furthermore, 3-dimethylaminopropenoates have been employed in the synthesis of 3-aminopyrrole-2,4-dicarboxylates,[4] 3-aminopyrrole-2-carboxylates[4] and pyrrole-2-carboxylates.[5a–c]

We have recently reported a new, efficient way of obtaining highly functionalised buta-1,3-dienes by [2+2] cycloaddition of electron-poor acetylenes to (*Z*)-2-acylamino-3-dimethylaminopropenoates.[6] In this way, we obtained a new group of 3-dimethylaminopropenoate reagents, i.e., (1*E*,3*E*)-1-(benzoylamino)-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylates **1**, with several reactive functional groups, thus enabling a wide range of further transformations.

So far, it has been shown that 3-dimethylaminopropenoates and related enaminones are very useful and versatile reagents in the synthesis of a wide variety of heterocyclic systems,[7a,b] including some natural products and their analogues, such as aplysinopsins,[8a,b] meridianines,[9a–c] dipodazines and tryprostatins.[10a–d]

In this paper, we present the transformations of (1*E*,3*E*)-1-(benzoylamino)-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylates **1** into highly functionalised pyridinone and pyrrole derivatives.

2. Results and discussion

When 4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylate **1a**[6] reacted with anilines **2a–f** in anhydrous methanol under reflux, substitution of the dimethylamino group took place yielding a mixture of (1*E*,3*E*) 4-(arylamino)buta-1,3-diene-1,2,3-tricarboxylates **3a–f** and (1*E*,3*Z*) 4-(arylamino)buta-1,3-diene-1,2,3-tricarboxylates **3′a–f**. In order to achieve cyclisation, the crude mixtures of **3** and **3′** were heated to reflux in a basic solution of KOH in ethanol producing di-*tert*-butyl 1-aryl-5-benzamido-6-oxo-1,6-dihydropyridine-3,4-dicarboxylates **4a–f** (Scheme 1). The disappearance of signals for the methyl ester in the ^{1}H NMR spectra of pyridines **4a–f** confirms that the cyclisation took place at the methyl ester group.

The mixtures of **3** and **3′** were not separated and were used in the following reaction as such. The structures and ratios of **3a–f** and **3′a–f** were confirmed by ^{1}H NMR spectroscopy and HRMS. From the ^{1}H NMR spectra it was also deduced that we were dealing with

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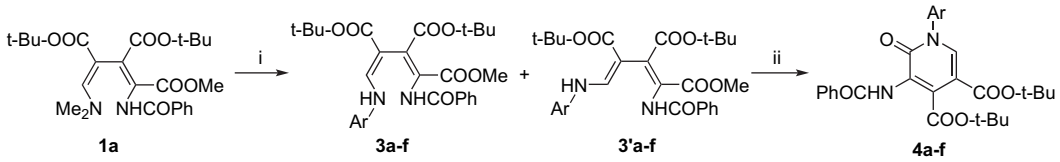
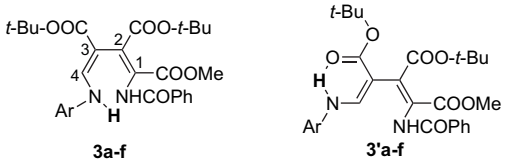


	Ar	**3** and **3'**, Yield (%)	**3 : 3'**	**4**, Yield (%),
a	Ph	98	63 : 37	68
b	4-Methylphenyl	96	50 : 50	69
c	4-Hydroxyphenyl	98	60 : 40	80
d	4-Fluorophenyl	91	59 : 41	66
e	3-Methoxyphenyl	98	54 : 46	72
f	1-Naphthyl	92	40 : 60	74

Scheme 1. Reagents and conditions: (i) anilines **2a**–**f**, anhydrous MeOH, reflux; (ii) KOH (~0.15 M), EtOH, reflux.



δ_{NH} = 6.8-7.5 ppm (no hydrogen bonding)

δ_{NH} = 10.21-11.17 ppm (hydrogen bonding)

Compound	δ (ppm) N*H*Ar	Compound	δ (ppm) N*H*Ar
3a	~6.8[a]	**3'a**	10.35
3b	~6.9[a]	**3'b**	10.30
3c	6.81	**3'c**	10.21
3d	~6.9[a]	**3'd**	10.34
3e	6.89	**3'e**	10.33
3f	~7.5[a]	**3'f**	11.17

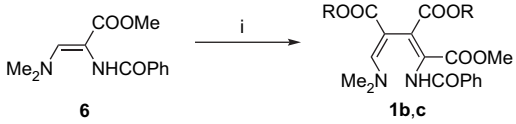
[a] Overlapped by other protons.

Figure 1.

isomers around the C(3)=C(4) double bond. The N*H*Ar signals of isomers **3a**–**f** appear at a higher field because no intramolecular hydrogen bonding is present, while the N*H*Ar signals of isomers **3′a**–**f** appear at much lower field due to intramolecular hydrogen bonding with one of the ester carbonyl groups (Fig. 1).

When a mixture of (1*E*,3*E*) 4-(arylamino)buta-1,3-diene-1,2,3-tricarboxylate **3a** and (1*E*,3*Z*) 4-(arylamino)buta-1,3-diene-1,2,3-tricarboxylate **3′a** was heated to reflux in a solution of KOH in methanol instead of ethanol, cyclisation into a pyridinone derivative was accompanied by removal of the benzoyl group producing di-*tert*-butyl 5-amino-6-oxo-1-phenyl-1,6-dihydropyridine-3,4-dicarboxylate (**5**) (Scheme 2).

The formation of pyridinone derivatives **4a**–**f** from 4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylate **1a** is probably due to a larger steric hindrance of the two *tert*-butyl esters in comparison with the methyl ester where the cyclisation takes place. This gives rise to a question, how would the cyclisation proceed with a compound with three methyl ester groups? In this manner, two new (1*E*,3*E*)-1-(benzoylamino)-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylates **1b**,**c** were prepared analogously to the literature procedure[6] (Scheme 3).



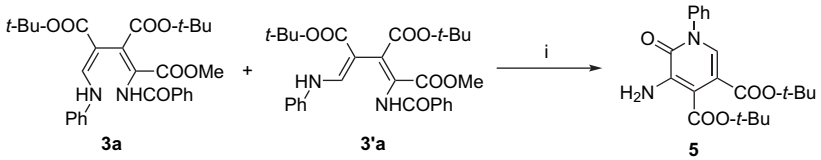
Compound	R	Yield (%)
1b	Me	93
1c	Et	94

Scheme 3. Reagents and conditions: (i) acetylenedicarboxylates **7a**,**b**, acetonitrile, microwave, 80 °C.

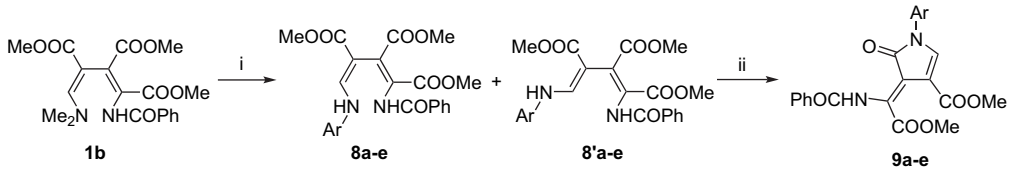
Reactions of anilines **2a**–**e** with trimethyl 4-(dimethylamino)-buta-1,3-diene-1,2,3-tricarboxylate **1b** in anhydrous methanol at reflux produced mixtures of (1*E*,3*E*) 4-(arylamino)buta-1,3-diene-1,2,3-tricarboxylates **8a**–**e** and (1*E*,3*Z*) 4-(arylamino)buta-1,3-diene-1,2,3-tricarboxylates **8′a**–**e**, as in the reactions of anilines **2a**–**f** with compound **1a** mentioned above. The yield of exchange products **8** and **8′** can be improved by use of a multiple excess of aniline **2**. When the crude mixtures of **8a**–**e** and **8′a**–**e** were stirred at room temperature in a solution of KOH in ethanol, formation of (*Z*)-methyl 4-(1-benzamido-2-methoxy-2-oxoethylidene)-5-oxo-1-aryl-4,5-dihydro-1*H*-pyrrole-3-carboxylates **9a**–**e** took place (Scheme 4).

Mixtures of **8a**–**e** and **8′a**–**e** were not separated. The structures and ratios of components were determined by ^{1}H NMR spectroscopy and HRMS. Again, ^{1}H NMR spectra revealed that we were dealing with isomers around the C(3)=C(4) double bond, where the N*H*Ar signals of isomers **8a**–**e** appear at a higher field than those of isomers **8′a**–**e**, due to the presence of intramolecular hydrogen bonding in the latter case (Fig. 2).

The determination of the structure of compounds **9a**–**e** was not as ambiguous as in the case of pyridinones **4a**–**f**. From the ^{1}H NMR spectra and the substantially different chemical shifts for the N*H*CO signals, it was clear that we were not dealing with pyridinone derivatives. In this case, the cyclisation proceeded on the ester group at position 2, resulting in the formation of pyrrole derivatives, which can exist as two isomers due to the exocyclic C=C double bond. The very high chemical shifts for N*H*CO protons indicate that (*Z*)-isomers are formed, where a very favourable six-membered ring hydrogen bond can be formed (Fig. 3). Additionally, the ^{13}C

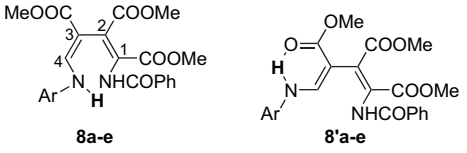


Scheme 2. Reagents and conditions: (i) KOH (0.13 M), MeOH, reflux.



	Ar	**8** and **8'**, Yield (%)	**8 : 8'**	**9**, Yield (%)
a	Ph	51	67 : 33	68
b	4-Methylphenyl	77	70 : 30	71
c	4-Hydroxyphenyl	73	73 : 27	63
d	4-Fluorophenyl	58	73 : 27	61
e	3-Methoxyphenyl	58	68 : 32	62

Scheme 4. Reagents and conditions: (i) anilines **2a**–**e**, anhydrous MeOH, reflux; (ii) KOH (~0.05 M), EtOH, rt.



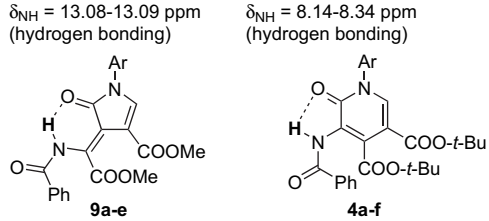
δ_{NH} = 6.97-7.11 ppm (no hydrogen bonding)

δ_{NH} = 10.29-10.40 ppm (hydrogen bonding)

Compound	δ (ppm) N*H*Ar	Compound	δ (ppm) N*H*Ar
8a	~7.0[a]	**8'a**	10.40
8b	~7.0[a]	**8'b**	10.36
8c	6.99	**8'c**	10.40
8d	7.11	**8'd**	10.39
8e	6.97	**8'e**	10.29

[a] Overlapped by other protons.

Figure 2.



δ_{NH} = 13.08-13.09 ppm (hydrogen bonding)

δ_{NH} = 8.14-8.34 ppm (hydrogen bonding)

Compound	δ (ppm) N*H*CO	Compound	δ (ppm) N*H*CO
9a	13.09	**6a**	8.25
9b	13.09	**6b**	8.25
9c	13.08	**6c**	8.14
9d	13.09	**6d**	8.22
9e	13.09	**6e**	8.24
-	-	**6f**	8.34

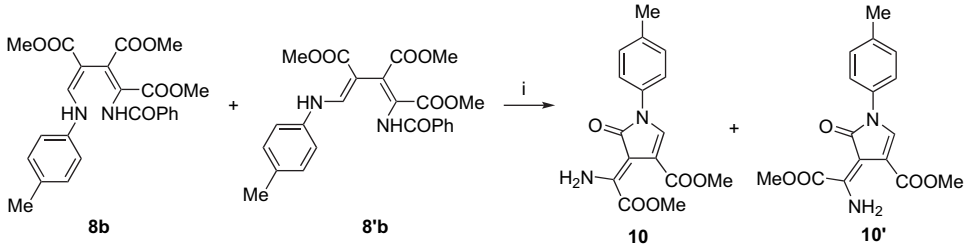
Figure 3.

NMR spectra of compounds **9a**–**e** exhibit four characteristic carbonyl signals, which confirm that compounds **9a**–**e** exist in the 5-oxo form. Furthermore, spectral data for compounds **9a**–**e** are in agreement with those of similar compound found in the literature.[3d,e]

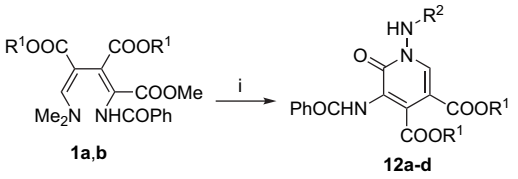
Similar to the cyclisation of the mixture of **3a** and **3′a** in methanol, when a mixture of (1*E*,3*E*) 4-(arylamino)buta-1,3-diene-1,2,3-tricarboxylate **8b** and (1*E*,3*Z*) 4-(arylamino)buta-1,3-diene-1,2,3-tricarboxylate **8′b** was stirred in a solution of KOH in methanol instead of ethanol, removal of the benzoyl group also took place forming (*Z*)-methyl 4-(1-amino-2-methoxy-2-oxoethylidene)-5-oxo-1-*p*-tolyl-4,5-dihydro-1*H*-pyrrole-3-carboxylate (**10**) and (*E*)-methyl 4-(1-amino-2-methoxy-2-oxoethylidene)-5-oxo-1-*p*-tolyl-4,5-dihydro-1*H*-pyrrole-3-carboxylate (**10′**) as an equimolar mixture (Scheme 5). The mixture of **10** and **10′** is unstable, therefore the structures were determined by ^{1}H NMR spectroscopy and HRMS.

In reactions of 4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylates **1a**,**c** with hydrazines **11a**,**b**, cyclisation products were formed in one step. In all cases, 1-arylamino-5-benzamido-6-oxo-1,6-dihydropyridine-3,4-dicarboxylates **12a**,**d** were formed (Scheme 6). While the cyclisation of **1a** with hydrazines **11a**,**b** proceeded on the methyl ester at position 1, the similarity of the ^{1}H NMR spectra of products obtained from **1b** with hydrazines **11a**,**b** confirms the same reaction pathway. Furthermore, the formation of diazepine derivative **13a** was ruled out by closer examination of the ^{1}H NMR spectra, where the N*H*R^2 protons appear at quite high chemical shifts due to intramolecular hydrogen bonding, which in diazepine derivatives would not be possible (Fig. 4). Additionally, the NMR signals for 2-H of the pyridinones **11a**–**d** appear as singlets, while signals for 3-H of the diazepine derivative **13a** would appear as doublets. The formation of **13b** is excluded due to easier exchange of the dimethylamino group in comparison to the reaction with the ester group.

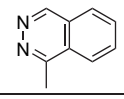
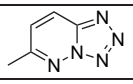
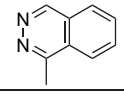
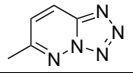
When *N*-aminopyridinone **12a** was heated to reflux in hydrazine monohydrate (**11c**), a derivative of pyrido[3,4-*c*]pyridazine **14** was formed (Scheme 7). Elemental analysis for C, H and N showed that compound **14** exists as a salt with hydrazine, which also explains its very high melting point.



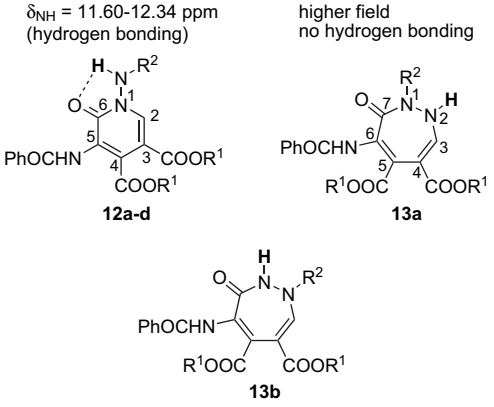
Scheme 5. Reagents and conditions: (i) KOH (0.06 M), MeOH, rt.



1a,b 12a-d

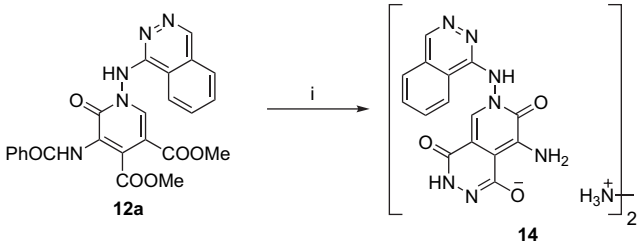
Compound	R^1	R^2	Yield (%)
12a	Me		76
12b	Me		84
12c	*t*-Bu		82
12d	*t*-Bu		86

Scheme 6. Reagents and conditions: (i) hydrazines **11a**,**b**, anhydrous MeOH, reflux.



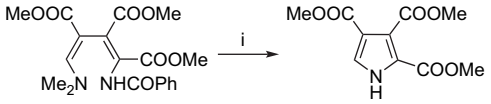
Compound	δ (ppm)		
	N*H*R^2	N*H*CO	2-H
12a	12.34	9.64	8.24
12b	11.65	9.97	8.66
12c	12.25	9.61	8.13
12d	11.60	9.91	8.48

Figure 4.



Scheme 7. Reagents and conditions: (i) hydrazine monohydrate (**11c**), reflux.

In the reactions of 4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylate **1b** with anilines we noticed when following the reactions by TLC that trimethyl 1*H*-pyrrole-2,3,4-tricarboxylate (**15**)[11] was always formed as a side product. The amount of this side product can be lowered by using anilines in excess. Pyrrole **15** was later separately prepared by intramolecular cyclisation of 4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylate **1b** in DMF by microwave irradiation (Scheme 8).



1b 15

Scheme 8. Reagents and conditions: DMF, microwave, 160 °C.

3. Conclusion

The reactivity of two highly functionalised (1*E*,3*E*)-1-(benzoylamino)-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylates **1a**,**b** towards various anilines **2a**–**f** and hydrazines **11a**,**b** was investigated. It has been shown that this new type of 3-dimethylaminopropenoate reagent **1** can easily be transformed into various highly substituted pyridinones **4** and **5**, *N*-aminopyridinones **12** and pyrroles **9**, **10** and **15**. Although, 4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylates **1** possess many reaction sites, it has been shown that reactions can be directed by selecting the appropriate starting compound to yield either pyridinone **4** or pyrrole **9** derivatives. Namely, different ester groups in the starting 4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylates **1** exhibit different steric hindrance. Due to their highly functionalised nature all newly formed compounds offer wide possibilities for further transformations.

4. Experimental

4.1. General

Melting points were determined on a Kofler micro hot stage. NMR spectra were obtained on a Bruker Avance DPX 300 at 300 MHz for ^{1}H, and 75.5 MHz for ^{13}C, using DMSO-d_6 and $CDCl_3$ as solvents and TMS as the internal standard. Microwave irradiations were performed on CEM Corporation Discover microwave unit. Mass spectra were recorded on an AutoSpecQ and Qtof-premier spectrometers, IR spectra on a Perkin–Elmer Spectrum BX FTIR spectrophotometer. Microanalyses were performed on a Perkin–Elmer CHN Analyser 2400 II. Column chromatography was performed on silica gel (Fluka, silica gel 60, 0.04–0.06 mm).

Anilines **2a**–**g**, acetylenes **7a**,**b**, hydrazines **11a**–**c** and KOH (85%) are commercially available (Sigma–Aldrich). (*Z*)-Methyl 2-benzamido-3-(dimethylamino)propenoate[12] (**6**) and 2,3-di-*tert*-butyl 1-methyl (1*E*,3*E*)-1-(benzoylamino)-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylate[6] (**1a**) were prepared according to the literature procedures.

4.2. General procedure for the synthesis of di-*tert*-butyl 1-aryl-5-benzamido-6-oxo-1,6-dihydropyridine-3,4-dicarboxylates 4a–f through (1*E*,3*E*)-2,3-di-*tert*-butyl 1-methyl 4-(arylamino)-1-(benzamido)buta-1,3-diene-1,2,3-tricarboxylates 3a–f and (1*E*,3*Z*)-2,3-di-*tert*-butyl 1-methyl 4-(arylamino)-1-(benzamido)buta-1,3-diene-1,2,3-tricarboxylates 3′a–f

Amine hydrochlorides **2a**–**f** (0.6–0.91 mmol, 1–1.2 equiv) were added to a solution of 2,3-di-*tert*-butyl 1-methyl (1*E*,3*E*)-1-(benzoylamino)-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylate (**1a**) (0.5–0.7 mmol) in dry methanol (2–3.5 ml). The reaction mixture was heated to reflux. Volatile components were evaporated in vacuo and the residue was purified by column chromatography on silica gel. Fractions containing the product were combined and evaporated in vacuo, which gave a yellow oily product. No further

purification of thus obtained mixture of (1*E*,3*E*)-2,3-di-*tert*-butyl 1-methyl 4-(arylamino)-1-(benzamido)buta-1,3-diene-1,2,3-tricarboxylates **3a–f** and (1*E*,3*Z*)-2,3-di-*tert*-butyl 1-methyl 4-(arylamino)-1-(benzamido)buta-1,3-diene-1,2,3-tricarboxylates **3′a–f** was undertaken. Potassium hydroxide (0.015–0.037 g) was added to a solution of crude mixture of **3a–f** and **3′a–f** (0.27–0.62 mmol) in ethanol (2–4 ml). The reaction mixture was heated to reflux and at the end neutralised with concentrated hydrochloric acid. Volatile components were evaporated in vacuo and the residue was purified by column chromatography on silica gel. Fractions containing the product were combined and evaporated in vacuo.

*4.2.1. (1E,3E)-2,3-Di-tert-butyl 1-methyl 4-(arylamino)-1-(benzamido)buta-1,3-diene-1,2,3-tricarboxylates **3a–f** and (1E,3Z)-2,3-di-tert-butyl 1-methyl 4-(arylamino)-1-(benzamido)buta-1,3-diene-1,2,3-tricarboxylates **3′a–f***

*4.2.1.1. (1E,3E)-2,3-Di-tert-butyl 1-methyl 1-benzamido-4-(phenylamino)buta-1,3-diene-1,2,3-tricarboxylate (**3a**) and (1E,3Z)-2,3-di-tert-butyl 1-methyl 1-benzamido-4-(phenylamino)buta-1,3-diene-1,2,3-tricarboxylate (**3′a**).* Prepared from **1a** (0.237 g, 0.5 mmol) and aniline hydrochloride (**2a**) (0.077 g, 0.6 mmol) in methanol (2 ml), 5.5 h, chromatography (ethyl acetate/petroleum ether=1:4). Yield: 0.255 g (98%) of yellow oil. ESI-MS: *m*/*z*=523.2 (MH^+), FABMS *m*/*z*=523 (MH^+). ^{1}H NMR ($CDCl_3$): *E*-isomer: δ 1.51 (9H, s, C(*Me*)$_3$), 1.52 (9H, s, C(*Me*)$_3$), 3.90 (3H, s, COO*Me*), 6.87–7.03 (4H, m, 3H of *Ph* and N*H*), 7.21–7.27 (2H, m, 2H of *Ph*), 7.32–7.55 (3H, m, 3H of *Ph*), 7.59 (1H, br s, N*H*CO), 7.63–7.68 (2H, m, 2H of *Ph*), 8.07 (1H, d, *J*=14.3 Hz, 4-*H*); *Z*-isomer: δ 1.50 (9H, s, C(*Me*)$_3$), 1.51 (9H, s, C(*Me*)$_3$), 3.92 (3H, s, COO*Me*), 6.87–7.03 (3H, m, 3H of *Ph*), 7.21–7.27 (2H, m, 2H of *Ph*), 7.32–7.55 (4H, m, 3H of *Ph* and 4-*H*), 7.71 (1H, br s, N*H*CO), 7.72–7.77 (2H, m, 2H of *Ph*), 10.35 (1H, br d, *J*=12.7 Hz, N*H*). Ratio of isomers: 63:37. ESI-HRMS: *m*/*z*=523.2450 (MH^+); $C_{29}H_{35}N_2O_7$ requires: *m*/*z*=523.2444 (MH^+); ν_{max} (KBr) 3377, 3292, 2979, 1737, 1718, 1661, 1624, 1601, 1587, 1505, 1476, 1367, 1299, 1272, 1250, 1156, 1127, 752, 714, 691 cm^{-1}.

*4.2.1.2. (1E,3E)-2,3-Di-tert-butyl 1-methyl 1-benzamido-4-(p-tolylamino)buta-1,3-diene-1,2,3-tricarboxylate (**3b**) and (1E,3Z)-2,3-di-tert-butyl 1-methyl 1-benzamido-4-(p-tolylamino)buta-1,3-diene-1,2,3-tricarboxylate (**3′b**).* Prepared from **1a** (0.316 g, 0.67 mmol) and *p*-toluidine hydrochloride (**2b**) (0.114 g, 0.67 mmol) in methanol (3 ml), 7 h, chromatography (ethyl acetate/petroleum ether=1:5). Yield: 0.342 g (96%) of yellow oil. ^{1}H NMR ($CDCl_3$): *E*-isomer: δ 1.50 (9H, s, C(*Me*)$_3$), 1.51 (9H, s, C(*Me*)$_3$), 2.26 (3H, s, Ph–*Me*), 3.91 (3H, s, COO*Me*), 6.77–6.87 (3H, m, 2H of *Ph* and N*H*), 7.00–7.07 (2H, m, 2H of *Ph*), 7.32–7.55 (3H, m, 3H of *Ph*), 7.59 (1H, br s, N*H*CO), 7.65–7.70 (2H, m, 2H of *Ph*), 8.04 (1H, d, *J*=14.4 Hz, 4-*H*); *Z*-isomer: δ 1.50 (9H, s, C(*Me*)$_3$), 1.51 (9H, s, C(*Me*)$_3$), 2.26 (3H, s, Ph–*Me*), 3.88 (3H, s, COO*Me*), 6.77–6.87 (2H, m, 2H of *Ph*), 7.00–7.07 (2H, m, 2H of *Ph*), 7.32–7.55 (4H, m, 3H of *Ph* and 4-*H*), 7.71 (1H, br s, N*H*CO), 7.72–7.77 (2H, m, 2H of *Ph*), 10.30 (1H, br d, *J*=13.2 Hz, N*H*). Ratio of isomers: 50:50. (Found: C, 66.90; H, 7.04; N, 5.27. $C_{30}H_{36}N_2O_7$ requires: C, 67.15; H, 6.76; N, 5.22.) ν_{max} (KBr) 3383, 3288, 1736, 1717, 1662, 1612, 1583, 1519, 1474, 1367, 1296, 1273, 1248, 1155, 1126, 713 cm^{-1}.

*4.2.1.3. (1E,3E)-2,3-Di-tert-butyl 1-methyl 1-benzamido-4-(4-hydroxyphenylamino)buta-1,3-diene-1,2,3-tricarboxylate (**3c**) and (1E,3Z)-2,3-di-tert-butyl 1-methyl 1-benzamido-4-(4-hydroxyphenylamino)buta-1,3-diene-1,2,3-tricarboxylate (**3′c**).* Prepared from **1a** (0.237 g, 0.5 mmol) and 4-hydroxyaniline hydrochloride (**2c**) (0.087 g, 0.6 mmol) in methanol (2 ml), 9 h, chromatography (ethyl acetate/petroleum ether=1:4). Yield: 0.255 g (98%) of yellow oil. FABMS *m*/*z*=539 (MH^+). ^{1}H NMR ($CDCl_3$): *E*-isomer: δ 1.50 (9H, s, C(*Me*)$_3$), 1.51 (9H, s, C(*Me*)$_3$), 3.88 (3H, s, COO*Me*), 5.54 (1H, s, O*H*), 6.66–6.76 (4H, m, 4H of *Ph*), 6.81 (1H, br d, *J*=15.6 Hz, N*H*), 7.33–7.56 (3H, m, 3H of *Ph*), 7.60 (1H, br s, N*H*CO), 7,64–7.69 (2H, m, 2H of *Ph*), 7.91 (1H, d, *J*=14.4 Hz, 4-*H*); *Z*-isomer: δ 1.50 (18H, s, 2×C(*Me*)$_3$), 3.91 (3H, s, COO*Me*), 5.53 (1H, s, O*H*), 6.66–6.76 (4H, m, 4H of *Ph*), 7.23 (1H, d, *J*=13.2 Hz, 4-*H*), 7.33–7.56 (3H, m, 3H of *Ph*), 7.72 (1H, br s, N*H*CO), 7.72–7.76 (2H, m, 2H of *Ph*), 10.21 (1H, br d, *J*=13.3 Hz, N*H*). Ratio of isomers: 60:40. (Found: C, 64.99; H, 6.75; N, 4.89. $C_{29}H_{34}N_2O_8$ requires: C, 64.67; H, 6.36; N, 5.20.) ν_{max} (KBr) 3375, 3303, 2979, 1717, 1658, 1622, 1597, 1518, 1476, 1368, 1301, 1269, 1251, 1155, 1130, 829, 713 cm^{-1}.

*4.2.1.4. (1E,3E)-2,3-Di-tert-butyl 1-methyl 1-benzamido-4-(4-fluorophenylamino)buta-1,3-diene-1,2,3-tricarboxylate (**3d**) and (1E,3Z)-2,3-di-tert-butyl 1-methyl 1-benzamido-4-(4-fluorophenylamino)buta-1,3-diene-1,2,3-tricarboxylate (**3′d**).* Prepared from **1a** (0.237 g, 0.5 mmol) and 4-fluoroaniline hydrochloride (**2d**) (0.096 g, 0.65 mmol) in methanol (2.5 ml), 7.5 h, chromatography (ethyl acetate/petroleum ether=1:4). Yield: 0.245 g (91%) of yellow oil. ESI-MS: *m*/*z*=541.2 (MH^+), FABMS *m*/*z*=541 (MH^+). ^{1}H NMR ($CDCl_3$): *E*-isomer: δ 1.50 (9H, s, C(*Me*)$_3$), 1.51 (9H, s, C(*Me*)$_3$), 3.88 (3H, s, COO*Me*), 6.82–6.98 (5H, m, 4H of *Ph* and N*H*), 7.30–7.56 (3H, m, 3H of *Ph*), 7.60 (1H, br s, N*H*CO), 7.64–7.69 (2H, m, 2H of *Ph*), 7.96 (1H, d, *J*=14.2 Hz, 4-*H*); *Z*-isomer: δ 1.50 (9H, s, C(*Me*)$_3$), 1.51 (9H, s, C(*Me*)$_3$), 3.91 (3H, s, COO*Me*), 6.82–6.98 (4H, m, 4H of *Ph*), 7.30–7.56 (4H, m, 3H of *Ph* and 4-*H*), 7.69 (1H, br s, N*H*CO), 7.73–7.77 (2H, m, 2H of *Ph*), 10.34 (1H, br d, *J*=13.0 Hz, N*H*). Ratio of isomers: 59:41. ESI-HRMS: *m*/*z*=541.2360 (MH^+); $C_{29}H_{34}FN_2O_7$ requires: *m*/*z*=541.2350 (MH^+); ν_{max} (KBr) 3384, 2979, 1733, 1717, 1663, 1624, 1599, 1514, 1475, 1367, 1298, 1273, 1251, 1226, 1155, 1128, 830, 713 cm^{-1}.

*4.2.1.5. (1E,3E)-2,3-Di-tert-butyl 1-methyl 1-benzamido-4-(3-methoxyphenylamino)buta-1,3-diene-1,2,3-tricarboxylate (**3e**) and (1E,3Z)-2,3-di-tert-butyl 1-methyl 1-benzamido-4-(3-methoxyphenylamino)buta-1,3-diene-1,2,3-tricarboxylate (**3′e**).* Prepared from **1a** (0.332 g, 0.7 mmol) and 2-methoxyaniline hydrochloride (**2e**) (0.145 g, 0.91 mmol) in methanol (3.5 ml), 6.5 h, chromatography (ethyl acetate/petroleum ether=1:4 and 1:3). Yield: 0.378 g (98%) of yellow oil. EIMS: *m*/*z*=552 (M^+). ^{1}H NMR ($CDCl_3$): *E*-isomer: δ 1.51 (9H, s, C(*Me*)$_3$), 1.51 (9H, s, C(*Me*)$_3$), 3.76 (3H, s, COO*Me*), 3.89 (3H, s, O*Me*), 6.23–6.58 (3H, m, 3H of *Ph*), 6.89 (1H, br d, *J*=13.9 Hz, N*H*), 7.13 (1H, t, *J*=8.1 Hz, 1H of *Ph*), 7.33–7.54 (3H, m, 3H of *Ph*), 7.59 (1H, br s, N*H*CO), 7.64–7.69 (2H, m, 2H of *Ph*), 8.04 (1H, d, *J*=14.2 Hz, 4-*H*); *Z*-isomer: δ 1.50 (9H, s, C(*Me*)$_3$), 1.50 (9H, s, C(*Me*)$_3$), 3.72 (3H, s, COO*Me*), 3.92 (3H, s, O*Me*), 6.23–6.58 (3H, m, 3H of *Ph*), 7.06 (1H, t, *J*=8.0 Hz, 1H of *Ph*), 7.33–7.54 (4H, m, 3H of *Ph* and 4-*H*), 7.71 (1H, br s, N*H*CO), 7.72–7.77 (2H, m, 2H of *Ph*), 10.33 (1H, br d, *J*=14.2 Hz, N*H*). Ratio of isomers: 54:46. EI-HRMS: *m*/*z*=522.2488 (M^+); $C_{30}H_{36}N_2O_8$ requires: *m*/*z*=522.2472 (M^+); ν_{max} (KBr) 3375, 3289, 2979, 1737, 1717, 1661, 1621, 1600, 1591, 1503, 1476, 1367, 1274, 1255, 1153, 1128, 1048, 842, 713, 688 cm^{-1}.

*4.2.1.6. (1E,3E)-2,3-Di-tert-butyl 1-methyl 1-benzamido-4-(naphthalen-1-ylamino)buta-1,3-diene-1,2,3-tricarboxylate (**3f**) and (1E,3Z)-2,3-di-tert-butyl 1-methyl 1-benzamido-4-(naphthalen-1-ylamino)buta-1,3-diene-1,2,3-tricarboxylate (**3′f**).* Prepared from **1a** (0.332 g, 0.7 mmol) and 1-naphthylamine hydrochloride (**2f**) (0.177 g, 0.91 mmol) in methanol (3.5 ml), 8 h, chromatography (ethyl acetate/petroleum ether=1:4). Yield: 0.367 g (92%) of yellow oil. EIMS: *m*/*z*=572 (M^+). ^{1}H NMR ($CDCl_3$): *E*-isomer: δ 1.53 (9H, s, C(*Me*)$_3$), 1.54 (9H, s, C(*Me*)$_3$), 3.93 (3H, s, COO*Me*), 7.11 (1H, d, *J*=7.5 Hz, 1H of *Ar*), 7.28–7.90 (12H, m, 11H of *Ar* and N*H*), 8.09 (1H, br s, N*H*CO), 8.17 (1H, d, *J*=13.6 Hz, 4-*H*); *Z*-isomer: δ 1.52 (9H, s, C(*Me*)$_3$), 1.55 (9H, s, C(*Me*)$_3$), 3.93 (3H, s, COO*Me*), 6.95 (1H, d, *J*=7.5 Hz, 1H of *Ar*), 7.28–7.90 (12H, m, 10H of *Ar*, N*H*CO and 4-*H*), 8.02–8.07 (1H, m, 1H of *Ar*), 11.17 (1H, br d, *J*=12.4 Hz, N*H*). Ratio of isomers: 40:60. EI-HRMS: *m*/*z*=572.2511 (M^+); $C_{33}H_{36}N_2O_7$ requires: *m*/*z*=572.2523 (M^+); ν_{max}

(KBr) 3397, 2978, 1739, 1716, 1660, 1634, 1612, 1596, 1579, 1473, 1367, 1298, 1251, 1152, 792, 771 cm^{-1}.

*4.2.2. Di-tert-butyl 1-aryl-5-benzamido-6-oxo-1,6-dihydropyridine-3,4-dicarboxylates **4a–f***

*4.2.2.1. Di-tert-butyl 5-benzamido-6-oxo-1-phenyl-1,6-dihydropyridine-3,4-dicarboxylate (**4a**).* Prepared from a mixture of **3a** and **3′a** (0.139 g, 0.266 mmol) and KOH (0.015 g, 0.23 mmol) in ethanol (2 ml), 40 min, $HCl_{(concd)}$ (one drop), chromatography (ethyl acetate/petroleum ether=1:3 and 1:2), recrystallised from toluene/*n*-heptane (4:1). Yield: 0.089 g (68%) of white crystals; mp 179–181 °C. ^{1}H NMR ($CDCl_3$): δ 1.55 (9H, s, C(*Me*)$_3$), 1.57 (9H, s, C(*Me*)$_3$), 7.36–7.57 (8H, m, 8H of *Ph*), 7.79 (1H, s, 2-*H*), 7.87–7.93 (2H, m, 2H of *Ph*), 8.25 (1H, s, N*H*). ^{13}C NMR ($CDCl_3$) δ 27.8, 28.0, 82.0, 83.3, 111.1, 125.5, 126.3, 127.5, 128.4, 129.1, 129.4, 131.9, 133.4, 135.5, 137.4, 139.6, 159.2, 162.4, 163.4, 165.8. (Found: C, 68.56; H, 6.37; N, 5.95. $C_{28}H_{30}N_2O_6$ requires: C, 68.56; H, 6.16; N, 5.71.) ν_{max} (KBr) 3434, 3269, 2980, 1727, 1718, 1702, 1676, 1646, 1506, 1475, 1368, 1327, 1287, 1255, 1153, 1123, 1028, 846, 707, 699 cm^{-1}.

*4.2.2.2. Di-tert-butyl 5-benzamido-6-oxo-1-p-tolyl-1,6-dihydropyridine-3,4-dicarboxylate (**4b**).* Prepared from a mixture of **3b** and **3′b** (0.330 g, 0.615 mmol) and KOH (0.037 g, 0.56 mmol) in ethanol (4 ml), 35 min, $HCl_{(concd)}$ (two drops), chromatography (ethyl acetate/petroleum ether=1:3), recrystallised from toluene/*n*-heptane (3:1). Yield: 0.213 g (69%) of white crystals; mp 172–176 °C. ^{1}H NMR ($CDCl_3$): δ 1.54 (9H, s, C(*Me*)$_3$), 1.56 (9H, s, C(*Me*)$_3$), 2.43 (3H, s, *Me*), 7.23–7.35 (4H, m, 4H of *Ph*), 7.41–7.49 (2H, m, 2H of *Ph*), 7.50–7.57 (1H, m, 1H of *Ph*), 7.77 (1H, s, 2-*H*), 7.88–7.93 (2H, m, 2H of *Ph*), 8.25 (1H, s, N*H*). ^{13}C NMR ($CDCl_3$) δ 21.1, 27.9, 28.1, 82.1, 83.2, 111.3, 125.6, 126.0, 127.6, 128.5, 130.1, 132.0, 133.6, 134.8, 137.2, 137.3, 139.4, 159.3, 162.6, 163.5, 165.8. (Found: C, 69.12; H, 6.58; N, 5.44. $C_{29}H_{32}N_2O_7$ requires: C, 69.03; H, 6.39; N, 5.55.) ν_{max} (KBr) 3309, 2979, 2931, 1721, 1686, 1659, 1510, 1479, 1426, 1369, 1330, 1298, 1250, 1159, 1097, 1028, 847, 708 cm^{-1}.

*4.2.2.3. Di-tert-butyl 5-benzamido-1-(4-hydroxyphenyl)-6-oxo-1,6-dihydropyridine-3,4-dicarboxylate (**4c**).* Prepared from a mixture of **3c** and **3′c** (0.240 g, 0.474 mmol) and KOH (0.027 g, 0.41 mmol) in ethanol (3 ml), 40 min, $HCl_{(concd)}$ (two drops), chromatography (ethyl acetate/petroleum ether=1:1 and ethyl acetate), recrystallised from toluene/*n*-heptane (8:1). Yield: 0.192 g (80%) of white crystals; mp 189–191 °C. ^{1}H NMR ($CDCl_3$): δ 1.53 (9H, s, C(*Me*)$_3$), 1.54 (9H, s, C(*Me*)$_3$), 6.79–6.85 (2H, m, 2H of *Ph*–OH), 7.05–7.11 (2H, m, 2H of *Ph*-OH), 7.43–7.50 (2H, m, 2H of *Ph*), 7.51–7.58 (1H, m, 1H of *Ph*), 7.82 (1H, s, 2-*H*), 7.88–7.94 (2H, m, 2H of *Ph*), 8.14 (1H, br s, N*H*), OH exchanged. ^{13}C NMR (DMSO-d_6): δ 27.4, 27.6, 81.5, 82.0, 107.3, 115.5, 125.0, 127.5, 127.7, 128.2, 131.1, 131.6, 133.5, 141.1, 142.1, 157.7, 159.3, 162.1, 162.6, 165.9. (Found: C, 66.14; H, 6.17; N, 5.55. $C_{28}H_{30}N_2O_7$ requires: C, 66.39; H, 5.97; N, 5.53.) ν_{max} (KBr) 3194, 2974, 1720, 1664, 1644, 1612, 1513, 1487, 1458, 1371, 1330, 1308, 1287, 1156, 1124, 1020, 845 cm^{-1}.

*4.2.2.4. Di-tert-butyl 5-benzamido-1-(4-fluorophenyl)-6-oxo-1,6-dihydropyridine-3,4-dicarboxylate (**4d**).* Prepared from a mixture of **3d** and **3′d** (0.181 g, 0.335 mmol) and KOH (0.019 g, 0.29 mmol) in ethanol (2 ml), 45 min, $HCl_{(concd)}$ (one drop), chromatography (ethyl acetate/petroleum ether=1:2), recrystallised from toluene/*n*-heptane (4:1). Yield: 0.113 g (66%) of white crystals; mp 185–187 °C. ^{1}H NMR ($CDCl_3$): δ 1.55 (9H, s, C(*Me*)$_3$), 1.56 (9H, s, C(*Me*)$_3$), 7.17–7.24 (2H, m, 2H of *Ph*), 7.34–7.40 (2H, m, 2H of *Ph*), 7.41–7.48 (2H, m, 2H of *Ph*), 7.50–7.57 (1H, m, 1H of *Ph*), 7.75 (1H, s, 2-*H*), 7.87–7.92 (2H, m, 2H of *Ph*), 8.22 (1H, br s, N*H*). ^{13}C NMR ($CDCl_3$): δ 27.8, 28.0, 82.1, 83.4, 111.0, 116.4 (d, *J*=23.1 Hz), 125.4, 127.6, 128.3 (d, *J*=8.6 Hz), 128.4, 131.9, 133.2, 135.5 (d, *J*=3.1 Hz), 136.4, 137.8, 159.3, 162.2, 162.5 (d, *J*=250 Hz), 163.4, 165.8. (Found: C, 66.39; H, 5.98; N, 5.34. $C_{28}H_{29}FN_2O_6$ requires: C, 66.13; H, 5.75; N, 5.51.) ν_{max} (KBr) 3447, 3280, 2980, 1718, 1676, 1654, 1508, 1478, 1369, 1330, 1287, 1252, 1155, 846, 706 cm^{-1}.

*4.2.2.5. Di-tert-butyl 5-benzamido-1-(3-methoxyphenyl)-6-oxo-1,6-dihydropyridine-3,4-dicarboxylate (**4e**).* Prepared from a mixture of **3e** and **3′e** (0.230 g, 0.416 mmol) and KOH (0.023 g, 0.35 mmol) in ethanol (2 ml), 65 min, $HCl_{(concd)}$ (one drop), chromatography (ethyl acetate/petroleum ether=1:3), recrystallised from toluene/*n*-heptane (5:1). Yield: 0.157 g (72%) of white crystals; mp 120–124 °C. ESI-MS: *m*/*z*=521.2 (MH^+). ^{1}H NMR ($CDCl_3$): δ 1.55 (9H, s, C(*Me*)$_3$), 1.56 (9H, s, C(*Me*)$_3$), 3.84 (3H, s, O*Me*), 6.89–6.96 (2H, m, 2H of *Ph*), 7.00–7.05 (1H, m, 1H of *Ph*), 7.40–7.48 (3H, m, 3H of *Ph*), 7.50–7.57 (1H, m, 1H of *Ph*), 7.77 (1H, s, 2-*H*), 7.88–7.93 (2H, m, 2H of *Ph*), 8.24 (1H, s, N*H*). ^{13}C NMR ($CDCl_3$): δ 27.8, 28.1, 55.5, 82.1, 83.3, 111.2, 112.1, 115.1, 118.4, 125.5, 127.5, 128.5, 130.3, 132.0, 133.4, 135.3, 137.4, 140.7, 159.1, 160.2, 162.4, 163.4, 165.8. EI-HRMS: *m*/*z*=521.2305 (MH^+); $C_{29}H_{33}N_2O_7$ requires: *m*/*z*=521.2288 (MH^+); ν_{max} (KBr) 3325, 2979, 1720, 1683, 1661, 1605, 1507, 1489, 1425, 1368, 1343, 1305, 1286, 1242, 1158, 1132, 1030, 847, 707 cm^{-1}.

*4.2.2.6. Di-tert-butyl 5-benzamido-1-(naphthalen-1-yl)-6-oxo-1,6-dihydropyridine-3,4-dicarboxylate (**4f**).* Prepared from a mixture of **3f** and **3′f** (0.260 g, 0.454 mmol) and KOH (0.025 g, 0.38 mmol) in ethanol (2 ml), 15 min, $HCl_{(concd)}$ (one drop), chromatography (ethyl acetate/petroleum ether=1:2), recrystallised from toluene/*n*-heptane (3:1). Yield: 0.182 g (74%) of white crystals; mp 196–198 °C. ^{1}H NMR ($CDCl_3$): δ 1.52 (9H, s, C(*Me*)$_3$), 1.61 (9H, s, C(*Me*)$_3$), 7.40–7.63 (8H, m, 8H of *Ar*), 7.76 (1H, s, 2-*H*), 7.87–7.93 (2H, m, 2H of *Ar*), 7.94–7.99 (1H, m, 1H of *Ar*), 8.00–8.05 (1H, m, 1H of *Ar*), 8.34 (1H, br s, N*H*). ^{13}C NMR ($CDCl_3$) δ 27.9, 28.0, 82.1, 83.4, 111.6, 122.0, 125.0, 125.4, 125.7, 126.9, 127.5, 127.8, 128.4, 128.6, 130.1, 131.9, 133.4, 134.1, 135.0, 136.3, 137.7, 159.4, 162.5, 163.5, 165.8. (Found: C, 71.20; H, 6.00; N, 5.32. $C_{32}H_{32}N_2O_6$ requires: C, 71.09; H, 5.97; N, 5.18.) ν_{max} (KBr) 3309, 2978, 1713, 1686, 1507, 1478, 1433, 1394, 1369, 1333, 1300, 1248, 1157, 844, 784, 712 cm^{-1}.

4.3. Di-*tert*-butyl 5-amino-6-oxo-1-phenyl-1,6-dihydropyridine-3,4-dicarboxylate (5)

Potassium hydroxide (0.026 g, 0.39 mmol) was added to a solution of crude mixture of (1*E*,3*E*)-2,3-di-*tert*-butyl 1-methyl 1-benzamido-4-(phenylamino)buta-1,3-diene-1,2,3-tricarboxylate (**3a**) and (1*E*,3*Z*)-2,3-di-*tert*-butyl 1-methyl 1-benzamido-4-(phenylamino)-buta-1,3-diene-1,2,3-tricarboxylate (**3′a**) (0.242 g, 0.463 mmol) in methanol (3 ml). The reaction mixture was heated to reflux for 4 h. Volatile components were evaporated in vacuo and the residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether=1:4). Fractions containing the product were combined and evaporated in vacuo. The product was recrystallised from a mixture of toluene and *n*-heptane (5:1). Yield: 0.116 g (65%) of white crystals; mp 146–149 °C. ^{1}H NMR ($CDCl_3$): δ 1.54 (9H, s, C(*Me*)$_3$), 1.59 (9H, s, C(*Me*)$_3$), 5.85 (2H, br s, N*H*$_2$), 7.17 (1H, s, 2-*H*), 7.35–7.40 (2H, m, 2H of *Ph*), 7.42–7.55 (3H, m, 3H of *Ph*). ^{13}C NMR ($CDCl_3$): δ 28.3, 28.4, 81.8, 82.8, 109.7, 113.7, 126.6, 127.2, 129.1, 129.7, 139.7, 140.6, 158.0, 164.6, 166.4. (Found: C, 65.23; H, 7.00; N, 7.37. $C_{21}H_{26}N_2O_5$ requires: C, 65.27; H, 6.78; N, 7.25.) ν_{max} (KBr) 3478, 3351, 2981, 1719, 1704, 1656, 1586, 1438, 1368, 1339, 1277, 1258, 1172, 1112, 1022, 847, 790, 692 cm^{-1}.

4.4. General procedure for the synthesis of (1*E*,3*E*)-1-amino-4-(dimethylamino)buta-1,3-dienes 1b,c

Acetylenes **7a**,**b** (2 mmol) were added to a solution of (*Z*)-methyl 2-benzamido-3-(dimethylamino)propenoate (**6**) (0.248 g, 1 mmol) in acetonitrile (4 mL) and the mixture was stirred in a closed vessel

under microwave irradiation at automatically controlled constant temperature. The reaction mixture was cooled. Volatile components were evaporated in vacuo and the residue was purified by column chromatography on silica gel. Fractions containing the product were combined and evaporated in vacuo.

*4.4.1. Trimethyl (1E,3E)-1-(benzoylamino)-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylate (**1b**)*

Prepared from (*Z*)-methyl 2-benzamido-3-(dimethylamino)propenoate (**6**) (0.248 g, 1 mmol) and dimethyl acetylenedicarboxylate (**7a**) (0.250 mL, 2 mmol), 80 °C, 100 min, chromatography (ethyl acetate/petroleum ether=1:1), crystallisation from ethyl acetate/petroleum ether (3:2). Yield: 0.364 g (93%) of yellow crystals; mp 92–94 °C. EIMS: *m*/*z*=390 (M^+). ^{1}H NMR ($CDCl_3$): δ 2.87 (6H, s, N*Me*$_2$), 3.67 (3H, s, COO*Me*), 3.75 (3H, s, COO*Me*), 3.90 (3H, 3, COO*Me*), 7.38 (1H, br s, N*H*), 7.44–7.50 (2H, m, 2H of *Ph*), 7.54–7.61 (1H, m, 1H of *Ph*), 7.61 (1H, s, 4-*H*), 7.72–7.76 (2H, m, 2H of *Ph*). ^{13}C NMR ($CDCl_3$): δ 51.4, 52.4, 52.8, 89.2, 118.6, 127.3, 128.9, 132.2, 132.7, 133.3, 151.1, 164.4, 164.4, 167.2, 168.8. EI-HRMS: *m*/*z*=390.1439 (M^+); $C_{19}H_{22}N_2O_7$ requires: *m*/*z*=390.1427 (M^+); ν_{max} (KBr) 3279, 2950, 2924, 1725, 1666, 1609, 1508, 1478, 1434, 1297, 1258, 1219, 1096, 775, 712 cm^{-1}.

*4.4.2. 2,3-Diethyl 1-methyl (1E,3E)-1-(benzoylamino)-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylate (**1c**)*

Prepared from (*Z*)-methyl 2-benzamido-3-(dimethylamino)propenoate (**6**) (0.248 g, 1 mmol) and diethyl acetylenedicarboxylate (**7b**) (0.325 mL, 2 mmol), 80 °C, 120 min, chromatography (ethyl acetate/petroleum ether=1:1). Yield: 0.395 g (94%) of yellow oil. EIMS: *m*/*z*=418 (M^+). ^{1}H NMR ($CDCl_3$): δ 1.22 (3H, t, *J*=7.1 Hz, CH_2CH_3), 1.28 (3H, t, *J*=7.1 Hz, CH_2CH_3), 2.85 (6H, s, N*Me*$_2$), 3.89 (3H, s, COO*Me*), 4.04–4.26 (4H, m, 2×CH_2CH_3), 7.31 (1H, br s, N*H*), 7.44–7.50 (2H, m, 2H of *Ph*), 7.54–7.76 (1H, m, 1H of *Ph*), 7.60 (1H, s, 4-*H*), 7.72–7.76 (2H, m, 2H of *Ph*). ^{13}C NMR ($CDCl_3$): δ 14.4, 14.7, 53.1, 60.5, 61.6, 90.2, 120.3, 127.7, 129.3, 132.6, 132.8, 133.0, 151.5, 164.9, 165.0, 167.3, 168.9. EI-HRMS: *m*/*z*=418.1751 (M^+); $C_{21}H_{26}N_2O_7$ requires: *m*/*z*=418.1740 (M^+); ν_{max} (NaCl) 3279, 2982, 2948, 1736, 1721, 1666, 1599, 1509, 1477, 1434, 1365, 1293, 1254, 1219, 1095, 1048, 774, 710 cm^{-1}.

4.5. General procedure for the synthesis of (*Z*)-methyl 4-(1-benzamido-2-methoxy-2-oxoethylidene)-5-oxo-1-aryl-4,5-dihydro-1*H*-pyrrole-3-carboxylates 9a–e through (1*E*,3*E*)-trimethyl 1-benzamido-4-(arylamino)buta-1,3-diene-1,2,3-tricarboxylates 8a–e and (1*E*,3*Z*)-trimethyl 1-benzamido-4-(arylamino)buta-1,3-diene-1,2,3-tricarboxylates 8′a–e

Amine hydrochlorides **2a**–**e** (1.8–4.0 mmol, 2.6–4 equiv) were added to a solution of (1*E*,3*E*)-trimethyl 1-benzamido-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylate (**1b**) (0.7–1.0 mmol) in dry methanol (2.5–3 ml). The reaction mixture was heated to reflux. After cooling to room temperature, the residual amine hydrochloride was filtered off and washed with CH_2Cl_2. Volatile components from the filtrate were evaporated in vacuo and the residue was purified by column chromatography on silica gel. Fractions containing the product were combined and evaporated in vacuo, which gave a yellow oily product. No further purification of thus obtained mixture of (1*E*,3*E*)-trimethyl 1-benzamido-4-(arylamino)buta-1,3-diene-1,2,3-tricarboxylates **8a**–**e** and (1*E*,3*Z*)-trimethyl 1-benzamido-4-(arylamino)buta-1,3-diene-1,2,3-tricarboxylates **8′a**–**e** was undertaken. Additionally, in some cases trimethyl 1*H*-pyrrole-2,3,4-tricarboxylate (**15**)[11] was isolated by column chromatography as a side product. Potassium hydroxide (0.005–0.009 g) was added to a solution of crude mixture of **8a**–**e** and **8′a**–**e** (0.36–0.70 mmol) in ethanol (1.5–2.5 ml). The reaction mixture was stirred at room temperature. The formed precipitate was filtered off under reduced pressure to give pure methyl 4-(1-benzamido-2-methoxy-2-oxoethylidene)-5-oxo-1-aryl-4,5-dihydro-1*H*-pyrrole-3-carboxylates **9a**–**e**.

*4.5.1. (1E,3E)-Trimethyl 1-benzamido-4-(arylamino)buta-1,3-diene-1,2,3-tricarboxylates **8a**–**e** and (1E,3Z)-trimethyl 1-benzamido-4-(arylamino)buta-1,3-diene-1,2,3-tricarboxylates **8′a**–**e***

*4.5.1.1. (1E,3E)-Trimethyl 1-benzamido-4-(phenylamino)buta-1,3-diene-1,2,3-tricarboxylate (**8a**) and (1E,3Z)-trimethyl 1-benzamido-4-(phenylamino)buta-1,3-diene-1,2,3-tricarboxylate (**8′a**).* Prepared from **1b** (0.390 g, 1 mmol) and aniline hydrochloride (**2a**) (0.389 g, 3 mmol) in methanol (2 ml), 8 h, chromatography (ethyl acetate/petroleum ether=2:3). Yield: 0.224 g (51%) of yellow oil. EIMS: *m*/*z*=438 (M^+). ^{1}H NMR ($CDCl_3$): *E*-isomer: δ 3.74 (3H, s, COO*Me*), 3.75 (3H, s, COO*Me*), 3.91 (3H, s, COO*Me*), 6.90–7.08 (4H, m, 3H of *Ph* and N*H*), 7.20–7.30 (2H, m, 2H of *Ph*), 7.32–7.55 (3H, m, 3H of *Ph*), 7.65–7.70 (2H, m, 2H of *Ph*), 7.79 (1H, br s, N*H*CO), 8.15 (1H, d, *J*=14.4 Hz, 4-*H*); *Z*-isomer: δ 3.74 (3H, s, COO*Me*), 3.75 (3H, s, COO*Me*), 3.94 (3H, s, COO*Me*), 6.90–7.08 (3H, m, 3H of *Ph*), 7.20–7.30 (2H, m, 2H of *Ph*), 7.32–7.55 (4H, m, 3H of *Ph* and 4-*H*), 7.71–7.76 (2H, m, 2H of *Ph*), 7.83 (1H, br s, N*H*CO), 10.4 (1H, br d, *J*=13.4 Hz, N*H*). Ratio of isomers: 67:33. EI-HRMS: *m*/*z*=438.1438 (M^+); $C_{23}H_{22}N_2O_7$ requires: *m*/*z*=438.1427 (M^+); ν_{max} (KBr) 3283, 2951, 1728, 1660, 1624, 1601, 1585, 1505, 1478, 1436, 1266, 1219, 1158, 1127, 754, 691 cm^{-1}.

*4.5.1.2. (1E,3E)-Trimethyl 1-benzamido-4-(p-tolylamino)buta-1,3-diene-1,2,3-tricarboxylate (**8b**) and (1E,3Z)-trimethyl 1-benzamido-4-(p-tolylamino)buta-1,3-diene-1,2,3-tricarboxylate (**8′b**).* Prepared from **1b** (0.390 g, 1 mmol) and 4-methylaniline hydrochloride (**2b**) (0.574 g, 4 mmol) in methanol (3 ml), 5 h, chromatography (ethyl acetate/petroleum ether=1:2). Yield: 0.349 g (77%) of yellow oil. ESI-MS: *m*/*z*=453.2 (MH^+). ^{1}H NMR ($CDCl_3$): *E*-isomer: δ 2.26 (3H, s, Ph–*Me*), 3.73 (3H, s, COO*Me*), 3.74 (3H, s, COO*Me*), 3.90 (3H, s, COO*Me*), 6.78–6.86 (2H, m, 2H of *Ph*), 6.95–7.08 (3H, m, 2H of *Ph* and N*H*), 7.33–7.56 (3H, m, 3H of *Ph*), 7.66–7.71 (2H, m, 2H of *Ph*), 7.83 (1H, br s, N*H*CO), 8.11 (1H, d, *J*=14.5 Hz, 4-*H*); *Z*-isomer: δ 2.28 (3H, s, Ph–*Me*), 3.73 (3H, s, COO*Me*), 3.75 (3H, s, COO*Me*), 3.94 (3H, s, COO*Me*), 6.78–6.86 (2H, m, 2H of *Ph*), 6.95–7.08 (2H, m, 2H of *Ph*), 7.33–7.56 (4H, m, 3H of *Ph* in 4-*H*), 7.71–7.76 (2H, m, 2H of *Ph*), 7.85 (1H, br s, N*H*CO), 10.36 (1H, br d, *J*=13.1 Hz, N*H*). Ratio of isomers: 70:30. ESI-HRMS: *m*/*z*=453.1648 (MH^+); $C_{24}H_{24}N_2O_7$ requires: *m*/*z*=453.1662 (MH^+); ν_{max} (KBr) 3284, 2951, 1731, 1686, 1662, 1610, 1582, 1519, 1475, 1436, 1293, 1263, 1218, 1125, 715 cm^{-1}.

*4.5.1.3. (1E,3E)-Trimethyl 1-benzamido-4-(4-hydroxyphenylamino)buta-1,3-diene-1,2,3-tricarboxylate (**8c**) and (1E,3Z)-trimethyl 1-benzamido-4-(4-hydroxyphenylamino)buta-1,3-diene-1,2,3-tricarboxylate (**8′c**).* Prepared from **1b** (0.390 g, 1 mmol) and 4-hydroxyaniline hydrochloride (**2c**) (0.437 g, 3 mmol) in methanol (2 ml), 8 h, chromatography (ethyl acetate/petroleum ether=3:2). Yield: 0.330 g (73%) of yellow oil. EIMS: *m*/*z*=454 (M^+). ^{1}H NMR ($CDCl_3$): *E*-isomer: δ 3.73 (3H, s, COO*Me*), 3.76 (3H, s, COO*Me*), 3.90 (3H, s, COO*Me*), 5.56 (1H, br s, O*H*), 6.66–6.78 (4H, m, 4H of *Ph*), 6.97 (1H, br d, *J*=14.6 Hz, N*H*), 7.30–7.54 (3H, m, 3H of *Ph*), 7.66–7.71 (2H, m, 2H of *Ph*), 7.82 (1H, br s, N*H*CO), 7.99 (1H, d, *J*=14.5 Hz, 4-*H*); *Z*-isomer: δ 3.73 (3H, s, COO*Me*), 3.76 (3H, s, COO*Me*), 3.93 (3H, s, COO*Me*), 5.56 (1H, br s, O*H*), 6.66–6.78 (4H, m, 4H of *Ph*), 7.30–7.54 (4H, m, 3H of *Ph* and 4-*H*), 7.72–7.77 (2H, m, 2H of *Ph*), 7.85 (1H, br s, N*H*CO), 10.29 (1H, br d, *J*=13.3 Hz, N*H*). Ratio of isomers: 73:27. EI-HRMS: *m*/*z*=454.1386 (M^+); $C_{23}H_{22}N_2O_8$ requires: *m*/*z*=454.1376 (M^+); ν_{max} (KBr) 3280, 2950, 1732, 1717, 1684, 1645, 1599, 1518, 1478, 1436, 1377, 1325, 1300, 1264, 1221, 1175, 1128, 987, 694 cm^{-1}.

*4.5.1.4. (1E,3E)-Trimethyl 1-benzamido-4-(4-fluorophenylamino)buta-1,3-diene-1,2,3-tricarboxylate (**8d**) and (1E,3Z)-trimethyl 1-benzamido-4-(4-fluorophenylamino)buta-1,3-diene-1,2,3-tricarboxylate*

(***8′d***). Prepared from **1b** (0.390 g, 1 mmol) and 4-fluoroaniline hydrochloride (**2d**) (0.443 g, 3 mmol) in methanol (2.5 ml), 8 h, chromatography (ethyl acetate/petroleum ether=2:3). Yield: 0.266 g (58%) of yellow oil. EIMS: *m*/*z*=456 (M^+). ^{1}H NMR ($CDCl_3$): *E*-isomer: *δ* 3.74 (3H, s, COO*Me*), 3.76 (3H, s, COO*Me*), 3.90 (3H, s, COO*Me*), 6.85–7.00 (4H, m, 4H of *Ph*), 7.11 (1H, br d, *J*=14.2 Hz, N*H*), 7.35–7.55 (3H, m, 3H of *Ph*), 7.66–7.71 (2H, m, 2H of *Ph*), 7.79 (1H, br s, N*H*CO), 8.05 (1H, d, *J*=14.3 Hz, 4-*H*); *Z*-isomer: *δ* 3.74 (3H, s, COO*Me*), 3.75 (3H, s, COO*Me*), 3.94 (3H, s, COO*Me*), 6.85–7.00 (4H, m, 4H of *Ph*), 7.35–7.55 (4H, m, 3H of *Ph* and 4-*H*), 7.71–7.76 (2H, m, 2H of *Ph*), 7.81 (1H, br s, N*H*CO), 10.39 (1H, br d, *J*=13.0 Hz, N*H*). Ratio of isomers: 73:27. EI-HRMS: *m*/*z*=456.1322 (M^+); $C_{23}H_{21}FN_2O_7$ requires: *m*/*z*=456.1333 (M^+); ν_{max} (KBr) 3294, 2952, 1731, 1693, 1661, 1624, 1599, 1514, 1476, 1436, 1296, 1266, 1209, 1159, 1126, 830, 779, 716 cm^{-1}.

*4.5.1.5. (1E,3E)-Trimethyl 1-benzamido-4-(3-methoxyphenylamino) buta-1,3-diene-1,2,3-tricarboxylate (**8e**) and (1E,3Z)-trimethyl 1-benzamido-4-(3-methoxyphenylamino)buta-1,3-diene-1,2,3-tricarboxylate (**8′e**).* Prepared from **1b** (0.273 g, 0.7 mmol) and 3-methoxyaniline hydrochloride (**2e**) (0.293 g, 1.8 mmol) in methanol (2 ml), 8 h, chromatography (ethyl acetate/petroleum ether=2:3). Yield: 0.190 g (58%) of yellow oil. EIMS: *m*/*z*=468 (M^+). ^{1}H NMR ($CDCl_3$): *E*-isomer: *δ* 3.75 (3H, s, COO*Me*), 3.76 (3H, s, O*Me*), 3.76 (3H, s, COO*Me*), 3.91 (3H, s, COO*Me*), 6.44–6.62 (2H, m, 2H of *Ph*), 6.99 (1H, br d, *J*=14.4 Hz, N*H*), 7.11–7.20 (1H, m, 1H of *Ph*), 7.33–7.55 (3H, m, 3H of *Ph*), 7.65–7.70 (2H, m, 2H of *Ph*), 7.75 (1H, br s, N*H*CO), 7.92–7.98 (1H, m, 1H of *Ph*), 8.14 (1H, d, *J*=14.3 Hz, 4-*H*); *Z*-isomer: *δ* 3.73 (3H, s, COO*Me*), 3.74 (3H, s, O*Me*), 3.75 (3H, s, COO*Me*), 3.95 (3H, s, COO*Me*), 6.23–6.33 (1H, m, 1H of *Ph*), 6.44–6.62 (2H, m, 2H of *Ph*), 7.11–7.20 (1H, m, 1H of *Ph*), 7.33–7.55 (4H, m, 3H of *Ph* and 4-*H*), 7.70–7.74 (2H, m, 2H of *Ph*), 7.83 (1H, br s, N*H*CO), 10.40 (1H, br d, *J*=13.0 Hz, N*H*). Ratio of isomers: 68:32. EI-HRMS: *m*/*z*=468.1544 (M^+); $C_{24}H_{24}N_2O_8$ requires: *m*/*z*=468.1533 (M^+); ν_{max} (KBr) 3285, 2950, 1732, 1717, 1681, 1646, 1601, 1590, 1505, 1474, 1435, 1267, 1199, 1156, 1124, 778, 689 cm^{-1}.

*4.5.2. (Z)-Methyl 4-(1-benzamido-2-methoxy-2-oxoethylidene)-5-oxo-1-aryl-4,5-dihydro-1H-pyrrole-3-carboxylates **9a–e***

*4.5.2.1. (Z)-Methyl 4-(1-benzamido-2-methoxy-2-oxoethylidene)-5-oxo-1-phenyl-4,5-dihydro-1H-pyrrole-3-carboxylate (**9a**).* Prepared from a mixture of **8a** and **8′a** (0.215 g, 0.49 mmol) and KOH (0.007 g, 0.11 mmol) in ethanol (1.5 ml), 120 min. Yield: 0.135 g (68%) of fluorescent yellow crystals; mp 241–242 °C. ^{1}H NMR ($CDCl_3$): *δ* 3.93 (3H, s, COO*Me*), 4.07 (3H, s, COO*Me*), 7.28–7.36 (1H, m, 1H of *Ph*), 7.40–7.48 (4H, m, 4H of *Ph*), 7.49–7.56 (2H, m, 2H of *Ph*), 7.57–7.64 (1H, m, 1H of *Ph*), 7.88 (1H, s, 2-*H*), 8.03–8.14 (2H, m, 2H of *Ph*), 13.09 (1H, s, N*H*). ^{13}C NMR ($CDCl_3$) *δ* 52.6, 53.4, 105.8, 106.6, 123.0, 127.4, 128.3, 128.8, 129.4, 132.0, 133.1, 135.5, 140.0, 141.3, 164.3, 164.6, 165.6, 166.0. (Found: C, 65.20; H, 4.64; N, 6.84. $C_{22}H_{18}N_2O_6$ requires: C, 65.02; H, 4.46; N, 6.89.) ν_{max} (KBr) 3479, 2958, 1752, 1713, 1692, 1667, 1609, 1516, 1488, 1397, 1338, 1267, 1237, 1225, 1198, 1087, 993, 747, 717, 708 cm^{-1}.

*4.5.2.2. (Z)-Methyl 4-(1-benzamido-2-methoxy-2-oxoethylidene)-5-oxo-1-p-tolyl-4,5-dihydro-1H-pyrrole-3-carboxylate (**9b**).* Prepared from a mixture of **8b** and **8′b** (0.317 g, 0.7 mmol) and KOH (0.008 g, 0.12 mmol) in ethanol (2 ml), 150 min. Yield: 0.300 g (71%) of fluorescent yellow crystals; mp 202–203 °C. ^{1}H NMR ($CDCl_3$): *δ* .36 (3H, s, Ph–*Me*), 3.92 (3H, s, COO*Me*), 4.06 (3H, s, COO*Me*), 7.21–7.25 (2H, m, 2H of *Ph*–Me), 7.30–7.34 (2H, m, 2H of *Ph*–Me), 7.49–7.55 (2H, m, 2H of *Ph*), 7.57–7.64 (1H, m, 1H of *Ph*), 7.84 (1H, s, 2-*H*), 8.04–8.13 (2H, m, 2H of *Ph*), 13.09 (1H, s, N*H*). ^{13}C NMR ($CDCl_3$): *δ* 20.9, 52.5, 53.2, 105.3, 106.6, 122.6, 128.1, 128.7, 129.7, 131.8, 132.9, 133.0, 137.1, 139.5, 141.5, 164.2, 164.4, 165.5, 165.9. (Found: C, 65.80; H, 4.94; N, 6.63. $C_{23}H_{20}N_2O_6$ requires: C, 65.71; H, 4.79; N, 6.66.) ν_{max} (KBr) 3447, 1749, 1719, 1693, 1664, 1606, 1513, 1489, 1395, 1336, 1238, 1196, 1085, 990, 707 cm^{-1}.

*4.5.2.3. (Z)-Methyl 4-(1-benzamido-2-methoxy-2-oxoethylidene)-1-(4-hydroxyphenyl)-5-oxo-4,5-dihydro-1H-pyrrole-3-carboxylate (**9c**).* Prepared from a mixture of **8c** and **8′c** (0.300 g, 0.660 mmol) and KOH (0.009 g, 0.14 mmol) in ethanol (2.5 ml), 65 min. Yield: 0.176 g (63%) of fluorescent yellow crystals; mp 258–260 °C. ^{1}H NMR ($CDCl_3$): *δ* 3.83 (3H, s, COO*Me*), 3.85 (3H, s, COO*Me*), 6.79–6.86 (2H, m, 2H of *Ph*–OH), 7.26–7.32 (2H, m, 2H of *Ph*–OH), 7.53–7.65 (2H, m, 2H of *Ph*), 7.68–7.75 (1H, m, 1H of *Ph*), 7.96–8.04 (2H, m, 2H of *Ph*), 8.23 (1H, s, 2-*H*), 9.69 (1H, s, Ph–*OH*), 13.09 (1H, s, N*H*). ^{13}C NMR (DMSO-d_6): *δ* 52.4, 52.5, 103.9, 106.6, 115.4, 125.1, 126.6, 127.7, 129.0, 131.6, 133.3, 138.0, 143.7, 156.5, 163.2, 163.8, 165.1, 165.8. (Found: C, 62.37; H, 4.51; N, 6.50. $C_{22}H_{18}N_2O_7$ requires: C, 62.56; H, 4.30; N, 6.63.) ν_{max} (KBr) 3363, 2964, 1750, 1702, 1687, 1662, 1608, 1519, 1448, 1395, 1348, 1269, 1240, 1193, 1090, 996, 834, 709 cm^{-1}.

*4.5.2.4. (Z)-Methyl 4-(1-benzamido-2-methoxy-2-oxoethylidene)-1-(4-fluorophenyl)-5-oxo-4,5-dihydro-1H-pyrrole-3-carboxylate (**9d**).* Prepared from a mixture of **8d** and **8′d** (0.250 g, 0.548 mmol) and KOH (0.006 g, 0.09 mmol) in ethanol (2 ml), 45 min. Yield: 0.142 g (61%) of fluorescent yellow crystals; mp 202–205 °C. ^{1}H NMR ($CDCl_3$): *δ* 3.93 (3H, s, COO*Me*), 4.06 (3H, s, COO*Me*), 7.08–7.17 (2H, m, 2H of *Ph*–F), 7.39–7.46 (2H, m, 2H of *Ph*–F), 7.49–7.56 (2H, m, 2H of *Ph*), 7.58–7.65 (1H, m, 1H of *Ph*), 7.82 (1H, s, 2-*H*), 8.08–8.13 (2H, m, 2H of *Ph*), 13.09 (1H, s, N*H*). ^{13}C NMR ($CDCl_3$): *δ* 52.6, 53.3, 105.8, 106.3, 116.2 (d, *J*=22.9 Hz), 124.9 (d, *J*=8.5 Hz), 128.2, 128.8, 131.5, (d, *J*=2.9 Hz), 131.8, 133.1, 140.2, 140.9, 161.3 (d, *J*=248 Hz), 164.1, 164.6, 165.5, 165.9. (Found: C, 62.47; H, 4.23; N, 4.44. $C_{22}H_{17}FN_2O_6$ requires: C, 62.26; H, 4.04; N, 4.48.) ν_{max} (KBr) 3447, 3143, 2951, 1745, 1715, 1677, 1610, 1512, 1488, 1396, 1340, 1264, 1241, 1222, 1085, 709 cm^{-1}.

*4.5.2.5. (Z)-Methyl 4-(1-benzamido-2-methoxy-2-oxoethylidene)-1-(3-methoxyphenyl)-5-oxo-4,5-dihydro-1H-pyrrole-3-carboxylate (**9e**).* Prepared from a mixture of **8e** and **8′e** (0.170 g, 0.363 mmol) and KOH (0.005 g, 0.08 mmol) in ethanol (2 ml), 120 min. Yield: 0.099 g (62%) of fluorescent yellow crystals; mp 173–175 °C. ^{1}H NMR ($CDCl_3$): *δ* 3.83 (3H, s, O*Me*), 3.93 (3H, s, COO*Me*), 4.07 (3H, s, COO*Me*), 6.86 (1H, ddd, *J*=0.8, 2.4, 8.4 Hz, 1H of *Ph*–OMe), 7.00 (1H, ddd, *J*=0.8, 1.9, 7.9 Hz, 1H of *Ph*–OMe), 7.06 (1H, dd, *J*=1.9, 2.3 Hz, 1H of *Ph*–OMe), 7.33 (1H, dd, *J*=7.9, 8.3 Hz, 1H of *Ph*–OMe), 7.49–7.56 (2H, m, 2H of *Ph*), 7.57–7.64 (1H, m, 1H of *Ph*), 7.86 (1H, s, 2-*H*), 8.08–8.14 (2H, m, 2H of *Ph*), 13.08 (1H, s, N*H*). ^{13}C NMR ($CDCl_3$) *δ* 52.6, 53.3, 55.5, 105.7, 106.7, 108.8, 113.1, 114.8, 128.3, 128.8, 130.0, 131.9, 133.1, 136.6, 139.8, 141.3, 160.2, 164.3, 164.6, 165.5, 166.0. (Found: C, 63.50; H, 4.85; N, 6.60. $C_{23}H_{20}N_2O_7$ requires: C, 63.30; H, 4.62; N, 6.42.) ν_{max} (KBr) 3447, 2953, 1747, 1717, 1695, 1671, 1607, 1514, 1490, 1397, 1335, 1260, 1227, 1219, 1087, 1001, 713 cm^{-1}.

4.6. (*Z*)-Methyl 4-(1-amino-2-methoxy-2-oxoethylidene)-5-oxo-1-*p*-tolyl-4,5-dihydro-1*H*-pyrrole-3-carboxylate (10) and (*E*)-methyl 4-(1-amino-2-methoxy-2-oxoethylidene)-5-oxo-1-*p*-tolyl-4,5-dihydro-1*H*-pyrrole-3-carboxylate (10′)

Potassium hydroxide (0.020 g, 0.30 mmol) was added to a solution of crude mixture of **8b** and **8′b** (0.150 g, 0.33 mmol) in methanol (2 ml). The reaction mixture was stirred at room temperature for 6 h. Volatile components were evaporated in vacuo and the residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether=1:2). Fractions containing the product were combined and evaporated in vacuo. Yield: 0.046 g (44%) of yellow oil; mp 60–72 °C. EIMS: *m*/*z*=316 (M^+). ^{1}H NMR ($CDCl_3$): *δ* 2.34 (3H, s, Ph–*Me*), 2.37 (3H, s, Ph–*Me*), 3.76 (3H, s, COO*Me*), 3.82 (3H, s, COO*Me*), 3.89 (3H, s, COO*Me*), 3.94 (3H, s, COO*Me*), 5.53 (1H,

br s, H_a–NH), 5.92 (1H, br, s, H_a–NH), 7.16–7.27 (4H, m, 4H of *Ph*), 7.31–7.40 (4H, m, 4H of *Ph*), 7.35 (1H, s, 2-*H*), 7.57 (1H, s, 2-*H*), 9.31 (1H, br, s, H_b-NH), 9.58 (1H, br, s, H_b-NH). Ratio of isomers: 50:50. EI-HRMS: *m*/*z*=316.1066 (M^+); $C_{16}H_{16}N_2O_5$ requires: *m*/*z*=316.1059 (M^+); ν_{max} (KBr) 3385, 3150, 2953, 1745, 1713, 1684, 1624, 1570, 1516, 1441, 1391, 1232, 1202, 1181, 1077, 942, 820, 768 cm^{-1}.

4.7. Reactions of (1*E*,3*E*)-1-(benzoylamino)-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylates 1a,b with hydrazines 11a,b

*4.7.1. Dimethyl 5-benzamido-6-oxo-1-(phthalazin-1-ylamino)-1,6-dihydropyridine-3,4-dicarboxylate (**12a**)*

1-Hydrazinophthalazine hydrochloride (**11a**) (0.196 g, 1 mmol) was added to a solution of trimethyl (1*E*,3*E*)-1-(benzoylamino)-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylate (**1b**) (0.390 g, 1 mmol) in methanol (5 ml). The reaction mixture was heated to reflux for 17 h and then allowed to cool to room temperature. The precipitated product was filtered under reduced pressure. Yield: 0.358 g (76%) of white crystals; mp 245–248 °C. EIMS: *m*/*z*=473 (M^+). ^{1}H NMR (DMSO-d_6): δ 3.73 (3H, s, COO*Me*), 3.75 (3H, s, COO*Me*), 7.46–7.52 (2H, m, 2H of *Ar*), 7.54–7.62 (1H, m, 1H of *Ar*), 7.82–7.94 (5H, m, 5H of *Ph*), 8.24 (1H, s, 2-*H*), 8.33 (1H, s, 1H of *Ar*), 8.39 (1H, d, *J*=7.6 Hz, 1H of *Ar*), 9.65 (1H, s, N*H*), 12.34 (1H, s, N*H*). ^{1}H NMR (DMSO-d_6/D_2O), δ 3.78 (3H, s, COO*Me*), 3.79 (3H, s, COO*Me*), 7.51–7.60 (2H, m, 2H of *Ar*), 7.60–7.68 (1H, m, 1H of *Ar*), 8.84–8.97 (5H, m, 5H of *Ph*), 8.34 (1H, s, 2-*H*), 8.38 (1H, s, 1H of *Ar*), 8.42 (1H, d, *J*=7.8 Hz, 1H of *Ar*). (Found: C, 60.92; H, 4.17; N, 14.73. $C_{24}H_{19}N_5O_6$ requires: C, 60.89; H, 4.05; N, 14.79.) EI-HRMS: *m*/*z*=473.1349 (M^+); $C_{24}H_{19}N_5O_6$ requires: *m*/*z*=475.1349 (M^+); ν_{max} (KBr) 3431, 3237, 2952, 1724, 1646, 1600, 1542, 1511, 1485, 1449, 1307, 1281, 1225, 1131, 1112, 1038, 781, 713 cm^{-1}.

*4.7.2. Dimethyl 5-benzamido-6-oxo-1-(tetrazolo[1,5-b]pyridazin-6-ylamino)-1,6-dihydropyridine-3,4-dicarboxylate (**12b**)*

6-Hydrazinotetrazolo[1,5-*b*]pyridazine hydrochloride (**11b**) (0.188 g, 1 mmol) was added to a solution of trimethyl (1*E*,3*E*)-1-(benzoylamino)-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylate (**1b**) (0.390 g, 1 mmol) in methanol (5 ml). The reaction mixture was heated to reflux for 14 h and then allowed to cool to room temperature. The precipitated product was filtered under reduced pressure. Yield: 0.388 g (84%) of white crystals; mp 228–230 °C. FABMS: *m*/*z*=465 (MH^+). ESI-MS: *m*/*z*=465.1 (MH^+). ^{1}H NMR (DMSO-d_6): δ 3.78 (3H, s, COO*Me*), 3.81 (3H, s, COO*Me*), 7.46–7.53 (2H, m, 2H of *Ph*), 7.50 (1H, d, *J*=9.6 Hz, 1H of *Ar*), 7.54–7.61 (1H, m, 1H of *Ph*), 7.88–7.92 (2H, m, 2H of *Ph*), 8.62 (1H, d, *J*=9.7 Hz, 1H of *Ar*), 8.66 (1H, s, 2-*H*), 9.97 (1H, s, N*H*), 11.65 (1H, br s, N*H*). ^{13}C NMR (DMSO-d_6): δ 52.5, 52.6, 105.6, 118.4, 125.8, 126.6, 127.6, 128.3, 131.8, 133.1, 140.3, 141.1, 145.2, 155.2, 157.3, 162.7, 164.1, 166.1. ESI-HRMS: *m*/*z*=465.1267 (MH^+); $C_{20}H_{17}N_8O_6$ requires: *m*/*z*=465.1271 (MH^+); ν_{max} (KBr) 3447, 3226, 2956, 1725, 1698, 1668, 1627, 1506, 1484, 1448, 1313, 1284, 1244, 782, 714 cm^{-1}.

*4.7.3. Di-tert-butyl 5-benzamido-6-oxo-1-(phthalazin-1-ylamino)-1,6-dihydropyridine-3,4-dicarboxylate (**12c**)*

1-Hydrazinophthalazine hydrochloride (**11a**) (0.066 g, 0.33 mmol) was added to a solution of 2,3-di-*tert*-butyl 1-methyl (1*E*,3*E*)-1-(benzoylamino)-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylate (**1a**) (0.158 g, 0.33 mmol) in methanol (1.5 ml). The reaction mixture was refluxed for 7.5 h and then allowed to cool to room temperature. The precipitated product was filtered under reduced pressure. Yield: 0.152 g (82%) of white crystals; mp 167–170 °C. FABMS: *m*/*z*=558 (MH^+). ESI-MS: *m*/*z*=558.2 (MH^+). ^{1}H NMR (DMSO-d_6): δ 1.41 (9H, s, C(*Me*)$_3$), 1.51 (9H, s, C(*Me*)$_3$), 7.45–7.52 (2H, m, 2H of *Ar*), 7.53–7.60 (1H, m, 1H of *Ar*), 7.81–7.97 (5H, m, 5H of *Ar*), 8.13 (1H, s, 2-*H*), 8.32 (1H, s, 1H of *Ar*), 8.40 (1H, d, *J*=7.5 Hz, 1H of *Ar*), 9.61 (1H, s, N*H*), 12.25 (1H, s, N*H*). ^{13}C NMR (DMSO-d_6): δ 27.5, 27.6, 81.0, 81.4, 107.6, 124.0, 124.4, 124.9, 126.6, 126.7, 127.6, 128.1, 131.5, 132.1, 133.1, 133.8, 138.4, 139.1, 139.9, 150.7, 156.2, 162.4, 163.1, 165.8. ESI-HRMS: *m*/*z*=558.2358 (MH^+); $C_{30}H_{32}N_5O_6$ requires: *m*/*z*=558.2353 (MH^+); ν_{max} (KBr) 3419, 3262, 2978, 1717, 1707, 1671, 1654, 1602, 1515, 1485, 1329, 1286, 1156, 1029, 848 cm^{-1}.

*4.7.4. Di-tert-butyl 5-benzamido-6-oxo-1-(tetrazolo[1,5-b]pyridazin-6-ylamino)-1,6-dihydropyridine-3,4-dicarboxylate (**12d**)*

6-Hydrazinotetrazolo[1,5-*b*]pyridazine hydrochloride (**11b**) (0.063 g, 0.33 mmol) was added to a solution of 2,3-di-*tert*-butyl 1-methyl (1*E*,3*E*)-1-(benzoylamino)-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylate (**1a**) (0.158 g, 0.33 mmol) in methanol (1.5 ml). The reaction mixture was heated to reflux for 6 h. Volatile components were evaporated in vacuo and the residue was purified by column chromatography on silica gel (ethyl acetate). Fractions containing the product were combined and evaporated in vacuo. The product was recrystallised from a mixture of ethyl acetate and *n*-heptane (3:1). Yield: 0.158 g (86%) of white crystals; mp decomposes above 158 °C. ^{1}H NMR (DMSO-d_6): δ 1.41 (9H, s, C(*Me*)$_3$), 1.52 (9H, s, C(*Me*)$_3$), 7.45–7.52 (2H, m, 2H of *Ph*), 7.49 (1H, d, *J*=9.6 Hz, 1H of *Ar*), 7.53–7.60 (1H, m, 1H of *Ph*), 7.90–7.95 (2H, m, 2H of *Ph*), 8.48 (1H, s, 2-*H*), 8.62 (1H, d, *J*=9.7 Hz, 1H of *Ar*), 9.91 (1H, s, N*H*), 11.60 (1H, br s, N*H*). ^{1}H NMR (DMSO-d_6/D_2O): δ 1.43 (9H, s, C(*Me*)$_3$), 1.52 (9H, s, C(*Me*)$_3$), 7.46–7.56 (3H, m, 3H of *Ar*), 7.58–7.65 (1H, m, 1H of *Ar*), 7.88–7.94 (2H, m, 2H of *Ar*), 8.50 (1H, s, 2-*H*), 8.53 (1H, d, *J*=9.6 Hz, 1H of *Ar*). ^{13}C NMR (DMSO-d_6): δ 102.9, 107.5, 120.1, 124.2, 124.5, 126.7, 126.8, 132.2, 133.1, 139.2, 141.3, 150.1, 153.0, 153.3, 160.2. (Found: C, 56.61; H, 5.35; N, 20.50. $C_{26}H_{28}N_8O_6$ requires: C, 56.93; H, 5.14; N, 20.43.) ν_{max} (KBr) 3447, 3232, 2980, 1721, 1683, 1676, 1506, 1482, 1370, 1331, 1290, 1249, 1155, 836, 711 cm^{-1}.

4.8. Hydrazine-1,2-diium di(8-amino-4,7-dioxo-6-(phthalazin-1-ylamino)-3,4,6,7-tetrahydropyrido[3,4-*d*]-pyridazin-1-olate) (14)

Dimethyl 5-benzamido-6-oxo-1-(phthalazin-1-ylamino)-1,6-dihydropyridine-3,4-dicarboxylate (**12a**) (0.473 g, 1 mmol) was dissolved in hydrazine monohydrate (**11c**) (2 ml). The reaction mixture was heated to reflux for 1.5 h and then allowed to cool to room temperature before adding water (5 ml). The precipitated product was filtered under reduced pressure and washed with water (2 ml). Yield: 0.274 g (76%) of yellow crystals; mp decomposes above 323 °C. EIMS: *m*/*z*=337 (MH^+ of the anionic part). ^{1}H NMR (DMSO-d_6): δ 3.60 (5H, br s, 5H×N*H*), 7.24 (2H, br s, 2H×N*H*), 7.28 (1H, s, 5-*H*), 7.81–7.94 (3H, m, 3H of *Ar*), 8.31 (1H, s, 1H of *Ar*), 8.40 (1H, d, *J*=7.5 Hz, 1H of *Ar*). (Found: C, 50.67; H, 3.89; N, 31.63. $C_{30}H_{26}N_{16}O_6$ requires: C, 50.99; H, 3.71; N, 31.71.) ν_{max} (KBr) 3463, 3319, 3136, 1639, 1606, 1559, 1540, 1484, 1470, 1430, 1358, 1274, 1255, 1189, 1154, 1094, 1076, 808, 773 cm^{-1}.

4.9. Trimethyl 1*H*-pyrrole-2,3,4-tricarboxylate (15)[11]

A solution of (1*E*,3*E*)-trimethyl 1-benzamido-4-(dimethylamino)buta-1,3-diene-1,2,3-tricarboxylate (**1b**) (0.130 g, 0.33 mmol) in DMF (3 ml) was stirred in a closed vessel under microwave irradiation (160 °C, 30 min). The reaction mixture was cooled. Volatile components were evaporated in vacuo and the residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether=1:1). Fractions containing the product were combined and evaporated in vacuo. Yield: 0.079 g (99%) of white crystals; mp 96–98 °C (literature mp 97–98 °C[11]). EIMS: *m*/*z*=241 (M^+). ^{1}H NMR ($CDCl_3$): δ 3.82 (3H, s, COO*Me*), 3.87 (3H, s, COO*Me*), 3.95 (3H, s, COO*Me*), 7.48 (1H, d, *J*=3.3 Hz, 5-*H*), 9.43 (1H, br s, N*H*). EI-HRMS:

m/z=241.0590 (M^+); $C_{10}H_{11}NO_6$ requires: m/z=241.0586 (M^+); ν_{max} (KBr) 3297, 3123, 1739, 1708, 1520, 1443, 1291, 1198, 1173, 1070, 1016, 787 cm^{-1}.

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References and notes

1. (a) Spitzner, D. Pyridines. In *Houben-Weyl: Science of Synthesis*; Black, D. StC., Ed.; Thieme: Stuttgart, 2006; Vol. 15, pp 11–284; (b) Keller, P. A. Pyridones and Related Systems. In *Houben-Weyl: Science of Synthesis*; Black, D. StC., Ed.; Thieme: Stuttgart, 2006; Vol. 15, pp 285–387; (c) Black, D. StC. 1*H*-Pyrroles. In *Houben-Weyl: Science of Synthesis*; Maas, G., Ed.; Thieme: Stuttgart, 2006; Vol. 9, pp 441–552; (d) Jones, G. Pyridines and their Benzo Derivatives: Synthesis. In *Comprehensive Heterocyclic Chemistry*; Boulton, A. J., McKillop, A., Eds.; Pergamon: Oxford, 1984; Vol. 2, pp 395–510; (e) Sundberg, R. J. Pyrroles and their Benzo Derivatives: Synthesis and Applications. In *Comprehensive Heterocyclic Chemistry*; Bird, W. C., Cheeseman, G. W. H., Eds.; Pergamon: Oxford, 1984; Vol. 4, pp 313–376; (f) Jones, G. Pyridines and their Benzo Derivatives: Synthesis. In *Comprehensive Heterocyclic Chemistry*; McKillop, A., Ed.; Pergamon: Oxford, 1996; Vol. 5, pp 167–243; (g) Sundberg, R. J. Pyrroles and their Benzo Derivatives: Synthesis. In *Comprehensive Heterocyclic Chemistry*; Bird, W. C., Ed.; Pergamon: Oxford, 1996; Vol. 2, pp 119–206.
2. (a) Tutonda, M.; Vanderzande, D.; Vekemans, J.; Toppet, S.; Hoornaert, G. *Tetrahedron Lett.* **1986**, *27*, 2509; (b) Tutonda, M.; Vanderzande, D.; Hendrix, M.; Hoornaert, G. *Tetrahedron* **1990**, *46*, 5715; (c) Tutonda, M. G.; Vandenberghe, S. M.; Van Aken, K. J.; Hoornaert, G. J. *J. Org. Chem.* **1992**, *57*, 2935; (d) Vandenberghe, S. M.; Buysens, K. J.; Meerpoel, L.; Loosen, P. K.; Toppet, S. M.; Hoornaert, G. J. *J. Org. Chem.* **1996**, *61*, 304.
3. (a) Blount, J. F.; Coffen, D. L.; Katonak, D. A. *J. Org. Chem.* **1978**, *43*, 3821; (b) tom Dieck, H.; Zettlitzer, M. *Chem. Ber.* **1987**, *120*, 795; (c) Witthaut, D.; Fröhich, R.; Schäfer, H. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 4212; (d) Xu, G.; Sayre, L. M. *J. Org. Chem.* **2002**, *67*, 3007; (e) Riggs, R. L.; Morton, C. J. H.; Slawin, A. M. Z.; Smith, D. M.; Westwood, N. J.; Austen, W. S. D.; Stuart, K. E. *Tetrahedron* **2005**, *61*, 11230.
4. Selič, L.; Stanovnik, B. *Helv. Chim. Acta* **1998**, *81*, 1634.
5. (a) Malešič, M.; Krbavčič, A.; Golobič, A.; Golič, L.; Stanovnik, B. *J. Heterocycl. Chem.* **1997**, *34*, 1757; (b) Selič, L.; Stanovnik, B. *Synthesis* **1999**, 479; (c) Toplak, R.; Svete, J.; Stanovnik, B.; Golič Grdadolnik, S. *J. Heterocycl. Chem.* **1999**, *36*, 225.
6. Uršič, U.; Grošelj, U.; Meden, A.; Svete, J.; Stanovnik, B. *Tetrahedron Lett.* **2008**, *49*, 3775.
7. (a) Stanovnik, B.; Svete, J. *Synlett* **2000**, 1077; (b) Stanovnik, B.; Svete, J. *Chem. Rev.* **2004**, *104*, 2433.
8. (a) Selič, L.; Jakše, R.; Lampič, K.; Golič, L.; Golič Grdadolnik, S.; Stanovnik, B. *Helv. Chim. Acta* **2000**, *83*, 2802; (b) Selič, L.; Stanovnik, B. *Tetrahedron* **2001**, *57*, 3159.
9. (a) Jakše, R.; Svete, J.; Stanovnik, B.; Golobič, A. *Tetrahedron* **2004**, *60*, 4601; (b) Časar, Z.; Bevk, D.; Svete, J.; Stanovnik, B. *Tetrahedron* **2005**, *61*, 7508; (c) Stanovnik, B.; Svete, J. *Mini-Rev. Org. Chem.* **2005**, *2*, 211.
10. (a) Wagger, J.; Bevk, D.; Meden, A.; Svete, J.; Stanovnik, B. *Helv. Chim. Acta* **2006**, *89*, 240; (b) Wagger, J.; Golič Grdadolnik, S.; Grošelj, U.; Meden, A.; Stanovnik, B.; Svete, J. *Tetrahedron: Asymmetry* **2007**, *18*, 464; (c) Wagger, J.; Grošelj, U.; Meden, A.; Svete, J.; Stanovnik, B. *Tetrahedron* **2008**, *64*, 2801; (d) Wagger, J.; Svete, J.; Stanovnik, B. *Synthesis* **2008**, 1436.
11. Nicolaus, R. A.; Mangoni, L. *Gazz. Chim. Ital.* **1956**, *86*, 358.
12. Yamato, E.; Okumura, K. (Tanabe Seiyaku Co., Ltd). Jpn. Kokai 75 58,063; *Chem. Abstr.* **1975**, *83*, 193075y.