Regiospecific Synthesis of 3H-Pyrido[2,3-b][1,4]diazepin-4(5H)-ones via Haloform Reaction with the Isolation of N^3-[3-Oxo-4,4,4-trichloroalk-1-en-1-yl]-2,3-diaminopyridine Intermediates

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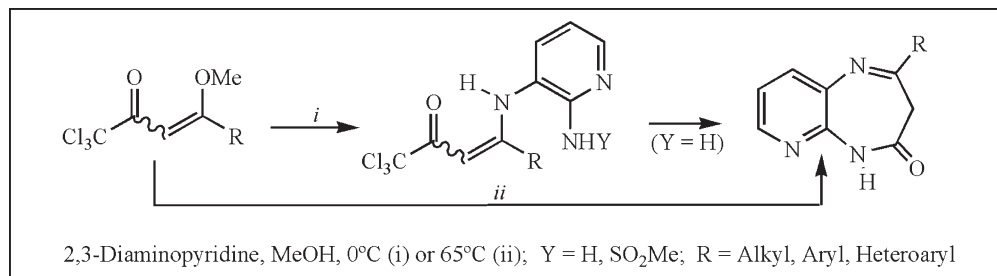Everton D. Deon, Nilo Zanatta, Alex F. C. Flores, and Marcos A. P. Martins

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2,3-Diaminopyridine, MeOH, 0°C (i) or 65°C (ii); Y = H, SO₂Me; R = Alkyl, Aryl, Heteroaryl

The synthesis of a novel series of analogous intermediates N^3-[1-alkyl(aryl/heteroaryl)-3-oxo-4,4,4-trichloroalk-1-en-1-yl]-2,3-diaminopyridines and N^2-(methanesulfonyl) [Cl₃CC(O)CH=CRNH(C₅H₃N)—NHY], where R = H, Me, C₆H₅, 4-FC₆H₄, 4-ClC₆H₄, 4-BrC₆H₄, 4-CH₃C₆H₄, 4-OCH₃C₆H₄, 4,4′-biphenyl, 1-naphthyl, 2-thienyl, 2-furyl, and Y = H, SO₂Me, is reported. A new corresponding series of 2-aryl/heteroaryl-3H-pyrido[2,3-b][1,4]diazepin-4(5H)-ones obtained from intramolecular cyclization reaction of the first series of trichloroacetyl enamines or from the direct cyclocondensation reaction of 4-methoxy-1,1,1-trichloalk-3-en-2-ones with 2,3-diaminopyridine, under mild conditions, is also demonstrated.

INTRODUCTION

The reactions of 2,3-diaminopyridine with ethyl benzoylacetate and ethyl nicotinoylacetate were first reported in a communication in 1964 by Barchet and Merz [1]. However, no evidence was given in support of the first 2-phenyl-1,3-dihydro-4H-pyrido[2,3-b][1,4]diazepin-4-one structure assignment.

Three years later, Israel *et al*. [2] found that different reaction conditions resulted in the preferential formation of dihydropyrido[2,3-b][1,4]diazepin-2-one or the 4-one isomer from the reaction of 2,3-diaminopyridine with ethyl acetoacetate. This reaction when conducted in boiling xylene for 8 h with azeotropic removal of water, afforded 2-methylpyrido[2,3-b][1,4]diazepin-4-one as the major product. However, 1,3-dihydro-1-isopropenyl-2H-imidazo[4,5-b]pyridin-2-one was present in small yield. In the absence of solvent, the mixture of 2,3-diaminopyridine with an excess of ethyl acetoacetate at 185°C for 15 min furnished 4-methylpyrido[2,3-b][1,4]diazepin-2-one, which was obtained as an inseparable tautomeric mixture of 1,3- and 1,5-dihydro-4-methyl-2H-pyrido[2,3-b][1,4]diazepin-2-one.

Later, in 1969, Israel and Jones [3] studied the reaction of 2,3-diaminopyridine with ethyl benzoylacetate in boiling xylene, in an approximation of the incompletely defined conditions given by Barchet and Merz [1] and obtained and proved the isolation of the same pyridodiazepinone described firstly in 1964.

In the 1960s, the determination of the correct structure for a given pyridodiazepinone product from the reaction involving 2,3-diaminopyridine and β-ketoesters was difficult and laborious, and, in some instances, an impossible task. Contributing with the solution of this problem, Israel and Jones [3,4] developed the thermal conversion of pyridodiazepinones into imidazolones, which permitted the assignment of the correct structures to ambiguous products through the knowledge that the N1—C2 bond of the pyridodiazepinone was not cleaved during the course of the rearrangement reaction.

Recently, various diamine-ketoester condensations involving reactions of ethyl 2-oxocyclohexanecarboxylate [5] or ethyl 2-oxocyclopentanecarboxylate [6] (cyclic β-ketoesters) with nonsymmetrical diaminopyridines have been studied, and the results compared in a attempt to develop generalizations of predictive value regarding the direction of ring closure to form diazepinones, as well as, in search of novel tricyclic ring systems which may be of interest in obtaining

clozapine and pirenzapine analogues with psychotropic properties.

Finally, in 2001 Savelli *et al*. [7] studied the reaction of 3-amino-2-(methylamino)pyridine with diethyl 1,3-acetonedicarboxylate to develop pyridodiazepinone derivatives. From the reaction mixture, Savelli separated dipyrido[1,2-*a*:2,3-*d*]imidazole derivatives as well as two isomeric pyrido[2,3-*b*]diazepinone derivatives in which the complex structural differentiation was achieved through NMR experiments and chemical evidence, but attempts to obtain the cited pyrido[2,3-*b*][1,4]diazepinone isomers as pure compounds have failed until now.

On the other hand, over the last few years, we have reported the synthesis of 2-trifluoro- and 2-trichloromethyl-3*H*-1,5-benzodiazepines from the reaction of 4-aryl-4-methoxy-1,1,1-haloalk-3-en-2-ones with *o*-phenylenediamine in good yields [8]. Next, we demonstrated that 4-phenyl-2-trichloromethyl-3*H*-1,5-benzodiazepine hydrogen sulfate possesses anxiolytic activity and produces motor in co-ordination similar to that observed in mice given diazepam [9]. In the same year, we also reported that some 4-substituted 2-trichloromethyl-3*H*-1,5-benzodiazepines presented an inhibitory effect on acetylcholinesterase and ATPDase activities from cerebral cortex of adult rats [10].

Recently, we have also reported an addition/elimination sequence leading to trichloroacetyl enamines from the reaction of *o*-phenylenediamine [8c] and *o*-aminophenol [11] with 4-alkyl(aryl)-1,1,1-trichloro-4-alkoxyalk-3-en-2-ones. Particularly, considering the importance of the development of new anticancer agents, in the last several years we have researched the possibility of using 4-alkoxy-1,1,1-trichloroalk-3-en-2-ones for the synthesis of new structures with promising chemotherapeutic potential. Thus, some acyclic trichloroacetyl enamines, derived from *o*-phenylenediamine and *o*-aminophenol, were submitted to *in vitro* antitumor screens and showed interesting results [11]. The best activity was obtained when the structure was derived from *o*-aminophenol and presented a *p*-bromophenyl substituent linked to the carbon-1 of the trichloromethylated enamino ketone.

In 2002, we showed the use of the trichloromethyl group as a convenient leaving group for the synthesis of 6-methyl- and 7-alkyl(aryl)-5H-thiazolo[3,2-*a*]pyrimidin-5-ones in 45–89% yields from the reaction of 4-alkyl(aryl)-1,1,1-trichloro-4-alkoxyalk-3-en-2-ones with 2-aminothiazole in refluxing ethanol [12]. In the mentioned work, it was only possible to isolate the non-substituted *N*-[3-oxo-4,4,4-trichlorobut-1-en-1-yl]-2-aminothiazole and all the other (1-substituted) enamino ketone intermediates *N*-[1-alkyl(aryl)-3-oxo-4,4,4-trichloroalk-1-en-1-yl]-2-aminothiazoles could be not isolated.

Recently, we have reported attempts to obtain *N*-[1-alkyl(aryl)-3-oxo-4,4,4-trichloroalk-1-en-1-yl]-2-ami-

nopyridine intermediates by the reaction of 4-alkoxy-1,1,1-trichloroalk-3-en-2-ones with 2-aminopyridine [13]. However, when these reactions were carried out in dichloromethane as solvent, under mild conditions, the respective trichloroacetyl enamines were isolated only in very low yields (>10%). Surprisingly, when the same reactions were carried out in a molar ratio of 1:1 in anhydrous ethanol as solvent under reflux for 5 h, 4-oxo-4*H*-pyrido[1,2-*a*]pyrimidines were easily isolated in 45–81% yields instead of *N*-[1-alkyl(aryl)-3-oxo-4,4,4-trichloroalk-1-en-1-yl]-2-aminopyridine intermediates.
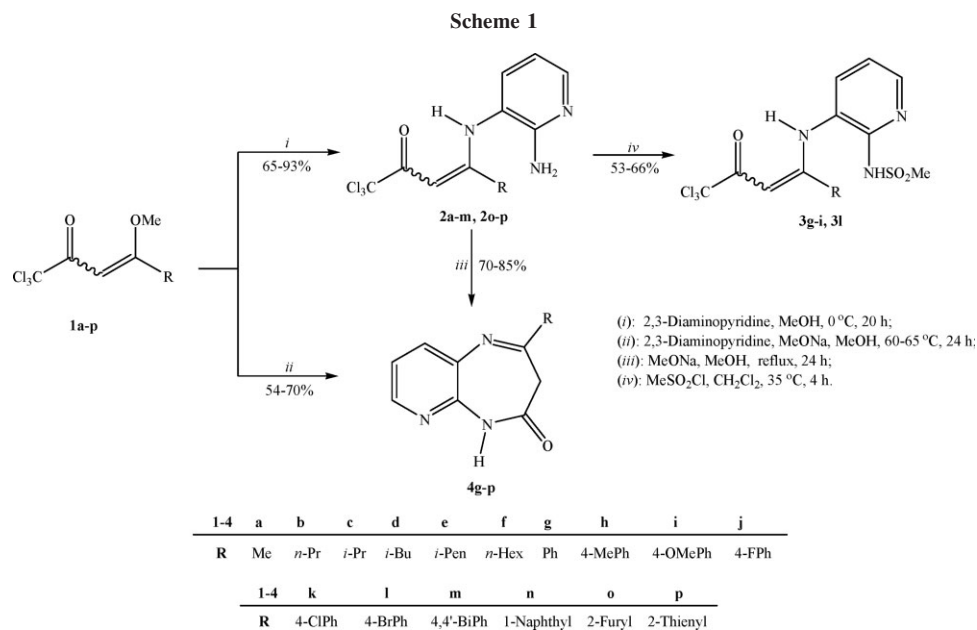
Surprisingly, since the first pyridodiazepinone was reported in 1964 [1], no publications have been found with the objective of carrying out a regiospecific and simultaneous introduction of trichloromethyl and substituted aryl groups at the pyrido[2,3-*b*][1,4]-diazepine derivatives starting from trichloromethyl substituted 1,3-diketones or 4-methoxy-1,1,1-trihaloalk-3-en-2-ones. In addition, there is no data on reactions involving simple 1,3-diketones, such as acetylacetone or benzoylacetone, with 2,3-diaminopyridine.

Only recently, we have communicated the first synthesis of 2-aryl(heteroaryl)-3*H*-pyrido[2,3-*b*][1,4]diazepin-4(5*H*)-ones from the direct cyclocondensation reaction of 4-methoxy-1,1,1-trichloroalk-3-en-2-ones (**1**) with 2,3-diaminopyridine [14].

Considering the biological importance of heterocyclic fused diazepinones and their derivatives and the fact that 2-aryl- and 2-heteroaryl-dihydropyridodiazepinone analogues and trichloroacetyl enamine intermediates have not yet been reported, it would be worthwhile to demonstrate a new synthetic application of β-aryl(heteroaryl)-β-methoxyvinyl trichloromethyl ketones. In addition, with the intention of carrying out future biological evaluations, it seemed desirable to develop a general method for the synthesis of pyridodiazepine derivatives (3*H*-1,5-benzodiazepine analogues), in which a trichloromethyl, carbonyl, aryl, or heteroaryl group could be introduced as substituent to this promising triaza fused heterocyclic family.

RESULTS AND DISCUSSION

Herein, the synthesis and isolation of a novel series of fifteen N^3-[1-aryl(heteroaryl)-3-oxo-4,4,4-trichloroalk-1-en-1-yl]-2,3-diaminopyridines and some N^3-[1-(aryl)-3-oxo-4,4,4-trichloroalk-1-en-1-yl]-N^2-(methanesulfonyl)-2,3-diaminopyridines and the regiospecific preparation of a series of 10 2-aryl(heteroaryl)-3*H*-pyrido[2,3-*b*][1,4]diazepin-4(5*H*)-ones from the intramolecular cyclization reaction of trichloroacetyl enamines, or direct cyclocondensation reaction of 4-substituted-4-methoxy-1,1,1-trichloroalk-3-en-2-ones with 2,3-diaminopyridine, is presented (Scheme 1).

Scheme 1

(*i*): 2,3-Diaminopyridine, MeOH, 0 °C, 20 h;
(*ii*): 2,3-Diaminopyridine, MeONa, MeOH, 60-65 °C, 24 h;
(*iii*): MeONa, MeOH, reflux, 24 h;
(*iv*): MeSO₂Cl, CH₂Cl₂, 35 °C, 4 h.

1-4	a	b	c	d	e	f	g	h	i	j
R	Me	*n*-Pr	*i*-Pr	*i*-Bu	*i*-Pen	*n*-Hex	Ph	4-MePh	4-OMePh	4-FPh

1-4	k	l	m	n	o	p
R	4-ClPh	4-BrPh	4,4'-BiPh	1-Naphthyl	2-Furyl	2-Thienyl

A review of the literature has shown that 2-methyl-and 2-phenyl-3*H*-pyrido[2,3-*b*][1,4]diazepin-4(5*H*)-ones, obtained under hard reaction conditions in boiling xylene, would result from the interaction of the more nucleophilic 3-amino group of the 2,3-diaminopyridine with the keto carbonyl function of the β-keto-ester [2]. This direction of cyclization was also seen in the cyclocondensation reaction of 2,3-diaminopyridine with ethyl benzoylacetate under similar conditions [3].

An extension of the reaction of ketones **1** with 2,3-diaminopyridine, a nonsymmetrical heteroaromatic diamine, necessarily introduces the additional problem of two possible isomeric diazepine products. The formation of the pyridodiazepine system presumably will depend on whether the initial reaction of the more nucleophilic 3-amino function occurs at the β-olefinic carbon of the vinyl ketones **1** or at the carbonyl carbon.

The ketones **1a** [15b], **1b-f** [12], **1g-j** [15a], **1m-n** [14], and **1o-p** [15g] are readily available *CCC* synthetic blocks and were prepared from trichloroacetylation reactions of enol ethers generated *in situ* from the respective aryl- or heteroaryl methyl ketone acetals [15] with trichloroacetyl chloride, respectively.

Subsequently, a novel series of 15 N^3-[1-alkyl(aryl/heteroaryl)-3-oxo-4,4,4-trichloroalk-1-en-1-yl]-2,3-diaminopyridines **2a-m**, **2o-p** was obtained in 65–93% yields by the methoxy-amino exchange reaction of **1** with 2,3-diaminopyridine and its X-ray diffraction data is shown (Fig. 1). The best results were obtained when the reactions of compounds **1a-p** with 2,3-diaminopyridine were carried out in methanol at 0°C for 20 h.

Crystallographic data for compound **2g**, reported in this article, have been given to the Cambridge Crystallographic Data Center (CCDC 687399) [16].

Initially, to obtain other new protected pyridino-sulfonamides bearing the similarly interesting aryl substituents at the enamino function, four examples of these new aryl-enamino ketones **2** were employed to obtain the respective N^3-[1-aryl-3-oxo-4,4,4-trichloroalk-1-en-1-yl]-N^2-(methanesulfonyl)-2,3-diaminopyridines (**3g-i**, **3l**). Thus, the reactions of **2g-i**, **2l** with methanesulfonyl chloride were carried out in dichlomethane as solvent at
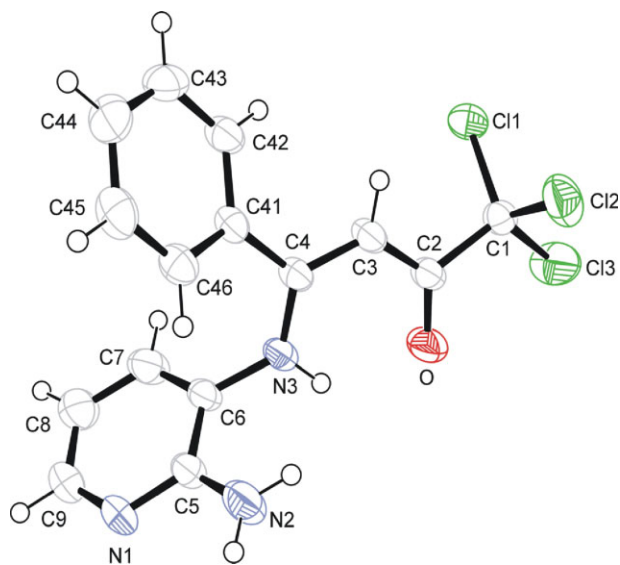

Figure 1. Perspective view of compound **2g**. Thermal ellipsoids correspond to 50% probability. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

35°C for 4 h. This procedure allowed for the easy attainment of sulfonamides **3g-i**, **3l** in 53–66% yields.

In this study, we also found that aryl- and heteroaryl-substituted trichloromethylated ketones **1g-p**, when treated directly with 2,3-diaminopyridine at a molar ratio of 1:1, respectively, in anhydrous methanol as solvent and in the presence of sodium methoxide under reflux for 24 h, regiospecifically produced 2-aryl(heteroaryl)-3*H*-pyrido[2,3-*b*][1,4]diazepin-4(5*H*)-ones (**4g-p**), which were easily isolated in 52–70% yields, as pure isomers. The above described conditions allowed us to regiospecifically obtain the diazepinones (**4**) instead of the analogous 2-aryl(heteroaryl)-4-trichloromethyl-4,5-dihydro-3*H*-pyrido[2,3-*b*][1,4]diazepin-4-ol or the respective 2-keto-pyridodiazepine isomers.

Although similar reaction conditions have been employed previously to synthesize 5*H*-thiazolo[2,3-*a*]pyrimidin-5-ones and 4*H*-pyrido[1,2-*a*]pyrimidin-4-ones, we found in this case an unexpected reactivity of the 2-amino group of the π-deficient pyridine ring toward the carbonyl group of the 4-aryl(heteroaryl)-4-methoxy-1,1,1-trichloroalk-3-en-2-ones (**2**), promoting an efficient haloform reaction. Compound **4g** had only been synthesized previously by Israel et al. [3] and by Barchet and Merz [1] in 65% yield from the reaction of 2,3-diaminopyridine with ethyl benzoylacetate, but under difficult reaction conditions (boiling xylene for 4 h with azeotropic distillation of the formed water). Our procedure not only gave the same compound under milder conditions (refluxing methanol for 24 h) and in a similar yield (52%) but also increased the scope of the reaction with the possibility of introducing other aryl and heteroaryl substituents to this pyridodiazepinone system.

Complementarily, examples of enamino ketones (**2g-m**, **2o-p**) were readily converted into **4g-m**, **4g-p** by refluxing in methanol in the presence of sodium methoxide for 24 h with yields higher than 70% (Scheme 1).

We consider the one-pot reaction presented to be a useful and convenient alternative to obtain regiospecifically pyridodiazepinone system and, in summary, the use of this methodology allowed also the isolation of two new series of N^3-[1-alkyl(aryl/heteroaryl)-3-oxo-4,4,4-trichloroalk-1-en-1-yl]-2,3-diaminopyridines and N^3-[1-aryl-3-oxo-4,4,4-trichloroalk-1-en-1-yl]-N^2-(methanesulfonyl)-2,3-diaminopyridines, which have been prepared in an analytically pure form and in good yields, for future chemical and biological studies.

EXPERIMENTAL

Unless otherwise indicated all common reagents and solvents were used as obtained from commercial suppliers without further purification. All melting points were determined on a calibrated Electrothermal Melt-Temp 3.0 apparatus. ^1H and ^{13}C

NMR spectra were acquired on a Bruker DPX 200 spectrometer (^1H at 200.13 MHz and ^{13}C at 50.32 MHz), 5mm sample tubes, 298 K, digital resolution ±0.01 ppm, in chloroform-d_1 (for **2**, **3**) or DMSO-d_6 (for **4**) using TMS as internal reference. The CHN elemental analyses were performed on a Perkin Elmer 2400 CHN elemental analyzer (São Paulo University–USP/Brazil).

General procedure for the preparation of substituted N^3-[3-oxo-4,4,4-trichloroalk-1-en-1-yl]-2,3-aminopyridines (2a-m, 2o-p). To a stirred solutions of 2,3-diaminopyridine (0.327 g, 3 mmol) in 10 mL of dry methanol, 4-alkoxy-4-aryl(alkyl)-1,1,1-trichloroalk-3-en-2-ones (**1a-m**, **1o-p**) (3 mmol) were added at 0°C. The mixtures were stirred for 20 h at 0°C. After the reaction time, yellow solids (**2a-m**, **2o-p**) were filtered, washed with cold methanol and recrystallized from hexane (yields 65–93%).

N^3-[4-Oxo-5,5,5-trichloropent-2-en-2-yl]-2,3-diaminopyridine (2a). Yield 86%; mp 120–122°C; ^1H NMR, δ (ppm) = 11.5 (s, 1H, NH), 8.0 (d, 1H, J = 5, PyH6), 7.3 (d, 1H, J = 7.5, PyH4), 6.70 (dd, 1H, J = 5, J = 5, PyH5), 5.9 (s, 1H, H2), 4.8 (s, 2H, NH₂), 2.1 (s, 3H, Me); ^{13}C NMR, δ (ppm) = 181.7 (C=O), 161.6 (C1), 154.9 (PyC2), 147.6 (PyC6), 135.6 (PyC4), 118 (PyC3), 113.9 (PyC5), 96.7 (CCl₃), 88.9 (C2), 20.2 (Me). Anal. Calcd. for C₁₀H₁₀Cl₃N₃O (mw 294.57): C, 40.77; H, 3.42; N,14.26%. Found: C, 40.56; H, 3.33; N, 14.17%.

N^3-[6-Oxo-7,7,7-trichlorohept-4-en-4-yl]-2,3-diaminopyridine (2b). Yield 65%; mp 147–149°C; ^1H NMR, δ (ppm) = 11.6 (s, 1H, NH), 8.0 (d, 1H, J = 5, PyH6), 7.3 (d, 1H, J = 7.5, PyH4), 6.72 (dd, 1H, J = 5, J = 5, PyH5), 6.0 (s, 1H, H2), 4.8 (s, 2H, NH₂), 2.2 (t, 2H, J = 8, CH₂), 1,1 (qui., 2H, J = 7, CH₂), 0.8 (t, 3H, J = 7, Me) ; ^{13}C NMR, δ (ppm) = 181.8 (C–O), 172.7 (C1), 155 (PyC2), 147.7 (PyC6), 135.8 (PyC4), 117.7 (PyC3), 113.8 (PyC5), 96.8 (CCl₃), 87.7 (C2), 34.5 (CH₂), 21.1 (CH₂), 13.6 (Me). Anal. Calcd. for C₁₂H₁₄Cl₃N₃O (mw 322.62): C, 44.60; H, 4.37; N, 13.02%. Found: C, 44.72; H, 4.41; N, 12.87%.

N^3-[2-Methyl-5-oxo-6,6,6-trichlorohex-3-en-3-yl]-2,3-diaminopyridine (2c). Yield 90%; mp 160–162 °C; ^1H NMR, δ (ppm) = 11.4 (s, 1H,NH), 7.9 (d, 1H, J = 5, PyH6), 7.4 (d, 1H, J = 7.5, PyH4), 6.71 (dd, 1H, J = 5, J = 5, PyH5), 6.1 (s, 2H, NH₂), 5.9 (s, 1H, H-2), 2.6 (qui., 1H, CH), 1.1 (d, 6H, J = 7, 2Me); ^{13}C NMR, δ (ppm) = 182.3 (C=O), 179.1 (C1), 155.3 (PyC2), 147.5 (PyC6), 136 (PyC4), 117.5 (PyC3), 113.8 (PyC5), 96.7 (CCl₃), 84.3 (C2), 29.9 (CH), 21.6 (2Me). Anal. Calcd. for C₁₂H₁₄Cl₃N₃O (mw 322.62): C, 44.60; H, 4.37; N, 13.02%. Found: C, 44.37; H, 4.17; N, 13.10%.

N^3-[2-Methyl-6-oxo-7,7,7-trichlorohept-4-en-4-yl]-2,3-diaminopyridine (2d). Yield 79%; mp 154–156°C; ^1H NMR, δ (ppm) = 11.5 (s, 1H, NH), 8.0 (d, 1H, J = 5, PyH6), 7.3 (d, 1H, J = 7.5, PyH4), 6.6 (dd, 1H, J = 5, J = 5, PyH5), 5.9 (s, 1H, H-2), 5.0 (s, 2H, NH₂), 2.2 (d, 4H, J = 8, CH₂), 1.8 (sex, 1H, CH), 0.8 (d, 6H, J = 7, 2Me); ^{13}C NMR, δ (ppm) = 181.3 (C=O), 171.7 (C1), 155.1 (PyC2), 147.2 (PyC6), 135.9 (PyC4), 117.6 (PyC3), 113.3 (PyC5), 96.7 (CCl₃), 88.4 (C2), 41.2 (CH₂), 27.4 (CH), 22.1 (Me). Anal. Calcd. for C₁₃H₁₆Cl₃N₃O (mw 336.65): C, 46.38; H, 4.79; N, 12.48%. Found: C, 46.49; H, 4.75; N, 12.37%.

N^3-[2-Methyl-7-oxo-8,8,8-trichlorooct-5-en-5-yl]-2,3-diaminopyridine (2e). Yield 93%; mp 132–135°C; ^1H NMR, δ (ppm) = 11.4 (s, 1H, NH), 8.0 (d, 1H, J = 5, PyH6), 7.4 (d, 1H, J = 7.5, PyH4), 6.72 (dd, 1H, J = 5, J = 5, PyH5), 5.9 (s, 1H, H2), 5.4 (s, 2H, NH₂), 2.2 (t, 2H, J = 7, CH₂), 1.5 (t, 2H,

J = 6, CH), 1.46–134 (m, 3H, CH$_2$ and CH), 0.8 (t, 3H, J = 7, 2Me); ^{13}C NMR, δ (ppm) = 181.8 (C=O), 173.4 (C1), 154.9 (PyC2), 147.6 (PyC6), 135.9 (PyC4), 117.7 (PyC3),113.8 (PyC5), 96.8 (CCl$_3$), 87.8 (C2), 36.9 (CH$_2$), 30.8 (CH), 27.8 (CH$_2$), 21.9 (Me). Anal. Calcd. for C$_{14}$H$_{18}$Cl$_3$N$_3$O (mw 350.68): C, 47.95; H, 5.17; N 11.98%. Found: C,48.13; H, 5.26; N, 12.22%.

N^3-[9-Oxo-10,10,10-trichlorodec-7-en-7-il]-2,3-diaminopyridine (2f). Yield 81%; mp 121–123°C; ^{1}H NMR, δ (ppm) = 11.4 (s, 1H, NH), 8.0 (d, 1H, J = 5, PyH6), 7.3 (d, 1H, J = 7.5, PyH4), 6.74 (dd, 1H, J = 5, J = 5, PyH5), 5.9 (s, 1H, H2), 5.0 (s, 2H, NH$_2$), 2.2 (t, J = 8, 2H, CH$_2$), 1.50–1.46 (m, 2H, CH$_2$), 1.24–1.19 (m, 6H, 3CH$_2$), 0.8 (t, J = 7, 3H, Me); ^{13}C NMR, δ (ppm) = 181.9 (C=O), 172.9 (C1), 154.8 (PyC2), 147 (PyC6), 136.2 (PyC4), 118 (PyC3), 113.8 (PyC5), 96.8 (CCl$_3$), 87.9 (C2), 32.6 (CH$_2$), 31.1 (CH$_2$), 28.7 (CH$_2$), 27.7 (CH$_2$), 22.3 (CH$_2$), 13.9 (Me). Anal. Calcd. for C$_{15}$H$_{20}$Cl$_3$N$_3$O (mw 364.70): C, 49.40; H, 5.53; N, 11.52%. Found: C, 49.63; H, 5.47; N, 11.57%.

N^3-[1-Phenyl-3-oxo-4,4,4-trichlorobut-1-en-1-yl]-2,3-diaminopyridine (2g). Yield 90%; mp 149–150°C; ^{1}H NMR, δ (ppm) = 11.4 (s, 1H, NH), 7.8 (d, 1H, J = 5, PyH6), 7.41–7.32 (m, 5H, Ph), 6.7 (d, 1H, J = 7.5, PyH4), 6.40 (dd, 1H, J = 5, J = 5, PyH5), 6.1 (s,1H, H2), 5.1 (s, 2H, NH$_2$); ^{13}C NMR, δ (ppm) = 182.3 (C=O), 167.6 (C1), 153.8 (PyC2), 144.8 (PyC6), 135.1 (PyC4), 133.9, 130.7, 128.7, 127.8 (4C, Ph), 119.9 (PyC3), 113.6 (PyC5), 96.6 (CCl$_3$), 91.3 (C2). Anal. Calcd. for C$_{15}$H$_{12}$Cl$_3$N$_3$O (mw 356.64): C, 50.52; H, 3.39; N, 11.78%. Found: C, 50.32; H, 3.31; N, 11.83%.

N^3-[1-(4-Methylphenyl)-3-oxo-4,4,4-trichlorobut-1-en-1-yl]-2,3-diaminopyridine (2h). Yield 73%; mp 174–175°C; ^{1}H NMR, δ (ppm) = 12.0 (s, 1H, NH), 7.8 (d, 1H, J =5, PyH6), 7.2 (d, 2H, ^3J = 8, Ph), 6.8 (d, 1H, ^3J = 8, Ph), 6.7 (d, 1H, J = 7.5, PyH4), 6.44 (dd, 1H, J = 5, J = 5, PyH5), 5.8 (s, 1H, H2), 5.3 (s, 2H, NH$_2$), 2.3 (s, 3H, Me); ^{13}C NMR, δ (ppm) = 168.0 (C=O), 153.8 (C1), 146.1 (PyC6), 145.2 (PyC2), 134.9 (PyC4), 129.4, 129.2, 128.8, 127.8 (4C, Ph), 119.9 (PyC3), 113.6 (PyC6), 92.7 (C2), 91.1 (CCl$_3$), 21.3 (Me). Anal. Calcd. for C$_{16}$H$_{14}$Cl$_3$N$_3$O (mw 370.67): C, 51.85; H, 3.81; N, 11.34%. Found: C, 51.70; H, 3.75; N, 11.13%.

N^3-[1-(4-Methoxyphenyl)-3-oxo-4,4,4-trichlorobut-1-en-1-yl]-2,3-diaminopyridine (2i). Yield 78%; mp 174–175°C; ^{1}H NMR, δ (ppm) = 11.5 (s, 1H, NH), 7.8 (d, 1H, J = 5, PyH6), 7.2 (d, 2H, ^3J = 9, Ph), 6.8 (d, 1H, ^3J = 9, Ph), 6.7 (d, 1H, J = 7.5, PyH4), 6.45 (dd, 1H, J = 5, J = 5, PyH5), 6.1 (s, 1H, H2), 4.9 (s, 2H, NH$_2$), 3.8 (s, 3H, OMe); ^{13}C NMR, δ (ppm) = 181.3 (C=O), 167.4 (C1), 161.5 (Ph), 153.7 (PyC2), 145.7 (PyC6), 134.6 (PyC4), 129.7, 125.8, 114.1 (3C, Ph), 120.1 (PyC3), 113.8 (PyC5), 96.8 (CCl$_3$), 90.8 (C2), 55.3 (OMe). Anal. Calcd. for C$_{16}$H$_{14}$Cl$_3$N$_3$O$_2$ (mw 386.67): C, 49.70; H, 3.65; N, 10.87%. Found: C, 49.95; H, 3.72; N, 10.60%.

N^3-[1-(4-Fluorophenyl)-3-oxo-4,4,4-trichlorobut-1-en-1-yl]-2,3-diaminopyridine (2j). Yield 80%; mp 146–148°C; ^{1}H NMR, δ (ppm) = 11.1 (s, 1H, NH), 7.8 (d, 1H, J = 5, PyH6), 7.3 (d, 2H, ^3J = 9, Ph), 7.0 (d, 2H, ^3J = 9, Ph), 6.8 (d, 1H, J = 7.5, PyH4), 6.4–6.3 (m, 1H, PyH5 and 2H, NH$_2$), 6.1 (s, 1H, H2); ^{13}C NMR, δ (ppm) = 182.2 (C=O), 166.5 (C1), 163.8 (d, $^1J_{CF}$ = 249.2, Ph), 153.8 (PyC2), 146.1 (PyC6), 134.8 (PyC4), 130.1 (d, $^3J_{CF}$ = 9, Ph), 129.9 (PyC3), 119.6 (d, $^2J_{CF}$ = 22, Ph), 116.0 (d, $^4J_{CF}$ = 3, Ph), 113.9 (PyC5), 96.6 (CCl$_3$), 91.3 (C2). Anal. Calcd. for C$_{15}$H$_{11}$Cl$_3$FN$_3$O (mw

374.63): C, 48.09; H, 2.96; N, 11.22%. Found: C, 48.21; H, 3.03; N, 11.15%.

N^3-[1-(4-Chlorophenyl)-3-oxo-4,4,4-trichlorobut-1-en-1-yl]-2,3-diaminopyridine (2k). Yield 67%; mp 180–182°C; ^{1}H NMR, δ (ppm) = 11.4 (s, 1H, NH), 7.9 (d, 1H, J = 5, PyH6), 7.4 (d, 2H, ^3J = 8, Ph), 7.2 (d, 2H, ^3J = 8, Ph), 6.7 (d, 1H, J = 7.5, PyH4), 6.46 (dd, 1H, J = 5, J = 5, PyH5), 6.1 (s, 1H, H2), 4.8 (s, 2H, NH$_2$); ^{13}C NMR, δ (ppm) = 182.5 (C=O), 165.9 (C1), 153.3 (PyC2), 142.9 (PyC6), 137.2 (Ph), 135.9 (PyC4), 132.1, 129.3, 129.2 (3C, Ph), 120.8 (PyC3), 113.5 (PyC5), 96.4 (CCl$_3$), 92.3 (C2). Anal. Calcd. for C$_{15}$H$_{11}$Cl$_4$N$_3$O (mw 391.08): C, 46.07; H, 2.84; N 10.74%. Found: C, 45.88; H, 2.87; N, 10.68%.

N^3-[1-(4-Bromophenyl)-3-oxo-4,4,4-trichlorobut-1-en-1-yl]-2,3-diaminopyridine (2l). Yield 93%; mp 182–184°C; ^{1}H NMR, δ (ppm) = 11.4 (s, 1H, NH), 7.9 (d, 1H, J = 5, PyH6), 7.4 (d, 2H, ^3J = 8, Ph), 7.2 (d, 2H, ^3J = 8, Ph), 6.7 (d, 1H, J = 7.5, PyH4), 6.47 (dd, 1H, J = 5, J = 5, PyH5), 6.1 (s, 1H, H2), 4.8 (s, 2H, NH$_2$); ^{13}C NMR, δ (ppm) = 179.9 (C=O), 165.9 (C1), 154.3 (PyC2), 143.1 (PyC6), 136.4 (PyC4), 133.6, 131.8, 129.9, 124.2 (4C, Ph), 120.2 (PyC3), 112.2 (PyC5), 96.6 (CCl$_3$), 90.2 (C2). Anal. Calcd. for C$_{15}$H$_{11}$Cl$_3$BrN$_3$O (mw 435.53): C, 41.37; H, 2.55; N 9.65%. Found: C, 41.50; H, 2.47; N, 9.94%.

N^3-[1-(4,4'-Biphenyl)-3-oxo-4,4,4-trichlorobut-1-en-1-yl]-2,3-diaminopyridine (2m). Yield 71%; mp 171–173°C; ^{1}H NMR, δ (ppm) = 11.5 (s, 1H, NH), 7.9 (d, 1H, J = 5, PyH6), 7.6–7.4 (m, 9H, Ph), 6.8 (d, 1H, J = 7.5, PyH4), 6.5 (dd, 1H, J = 5, J = 5, PyH5), 6.2 (s, 1H, H2), 4.9 (s, 2H, NH$_2$); ^{13}C NMR, δ (ppm) = 182.2 (C=O), 167.3 (C1), 153.8 (PyC2), 146.2 (PyC6), 143.5, 139.4, 132.6, 128.9, 128.5, 128.1, 127.2, 126.9 (8C, Ph), 134.6 (PyC4), 119.8 (PyC3), 113.9 (PyC5),96.7 (CCl$_3$), 91.3 (C2). Anal. Calcd. for C$_{13}$H$_{10}$Cl$_3$N$_3$O$_2$ (mw 346.60): C, 45.05; H, 2.91; N, 12.12%. Found: C, 45.17; H, 3.13; N, 12. 25%.

N^3-[1-(2-Furyl)-3-oxo-4,4,4-trichlorobut-1-en-1-yl]-2,3-diaminopyridine (2o). Yield 75%; mp 167–169°C; ^{1}H NMR, δ (ppm) =11.4 (s, 1H, NH), 7.8 (bs, 1H, PyH6), 7.2 (d, 1H, J = 4, fr), 7.1 (t, 1H, J = 4, fr), 7.0 (d, 1H, J = 4, fr), 6.9 (d, 1H, J = 7.5, PyH4), 6.41 (dd, 1H, J = 5, J = 5, PyH5), 6.1 (s, 1H, H2), 4.8 (s, 2H, NH$_2$); ^{13}C NMR, δ (ppm) = 182.3 (C=O), 167.3 (C1), 153.7 (PyC2),146 (PyC6), 139.5 (fr), 132.6 (PyC4), 128.9, 128.1, 127.3 (3C, fr), 119.9 (PyC3), 114.1 (PyC5), 96.7 (CCl$_3$), 91.4 (C2). Anal. Calcd. for C$_{19}$H$_{14}$Cl$_3$N$_3$O (mw 406.70): C, 56.11; H, 3.47; N, 10.33%. Found: C, 56.37; H, 3.46; N, 10.40%.

N^3-[1-(2-Thienyl)-3-oxo-4,4,4-trichlorobut-1-en-1-yl]-2,3-diaminopyridine (2p). Yield 79%; mp 175–177°C; ^{1}H NMR, δ (ppm) =11.4 (s, 1H, NH), 7.9 (d, 1H, J = 5, PyH6), 7.3 (d, 1H, J = 5, tn), 7.1 (d, 1H, J = 3, tn), 7.0 (d, 1H, J = 7, tn), 6.5 (d, 1H, J = 7.5, PyH4), 6.4 (dd, 1H, J = 5, J = 5, PyH5), 6.1 (s, 1H, H2), 5.2 (s, 2H, NH$_2$); ^{13}C NMR, δ (ppm) = 182.1 (C=O), 160.3 (C1), 154.6 (PyC2), 147.2 (PyC6), 135.8 (PyC4), 130.2, 127.7, 127.3 (3C, tn), 119.3 (PyC3), 114.1 (PyC5), 103.7 (CCl$_3$), 89.3 (C2). Anal. Calcd. for C$_{21}$H$_{16}$Cl$_3$N$_3$O (mw 432.74): C, 58.29; H, 3.73; N, 9.71%. Found: C, 58.32; H, 3.76; N, 9.66%.

General procedure for the preparation of substituted N^3-[1-alkyl(aryl/heteroaryl)-3-oxo-4,4,4-trichloroalk-1-en-1-yl]-N^2-(methanesulfonyl)-2,3-diaminopyridines (3g-i, 3l). To a stirred solutions of N^3-[1-aryl(heteroaryl)-3-oxo-4,4,4-

trichlorobut-1-en-1-yl]-2,3-diaminopyridines (**2g-i, 2l**) (1 mmol) in 5 mL of dry dichloromethane, pure methanesulfonyl chloride (0.15 mL, 2 mmol) was added at room temperature. The mixtures were stirred for 4 more hours at 35°C. After the reaction time, the reactions were filtered and the organic solvent was removed under reduced pressure. The crude yellow solids (**3g-i, 3l**) were recrystallized from hexane (yields 53–66%).

N³-[1-Phenyl-3-oxo-4,4,4-trichlorobut-1-en-1-yl]-N²-(methanesulfonyl)-2,3-diamino-pyridine (3g). Yield 63%; mp 168–170°C; ¹H NMR, δ (ppm) =10.9 (s, 1H, NH), 8.3 (s, 1H, NH), 7.6 (d, 1H, $J = 5$, PyH6), 7.42–7.28 (m, 5H, Ph), 7.0 (d, 1H, $J = 7.5$, PyH4), 6.5 (dd, 1H, $J = 5$, $J = 5$, PyH5), 6.1 (s, 1H, H2), 2.8 (s, 3H, Me); ¹³C NMR, δ (ppm) = 182.6 (C=O), 164.5 (C1), 145.1 (PyC6), 140.9 (PyC2), 135.1 (Ph), 133.9 (PyC4), 131.1 (PyC3), 129.2, 128.3, 124.8 (3C, Ph), 111.7 (PyC5), 96.3 (CCl₃), 93.8 (C2), 43.5 (Me). Anal. Calcd. for $C_{22}H_{18}Cl_3N_3O_3S$ (mw 510.82): C, 51.73; H, 3.55; N, 8.23%. Found: C, 52.01; H, 3.60; N, 8.33%.

N³-[1-(4-Methylphenyl)-3-oxo-4,4,4-trichlorobut-1-en-1-yl]-N²-(methanesulfonyl)-2,3-diaminopyridine (3h). Yield 53%; mp 174–176°C; ¹H NMR, δ (ppm) =11.0 (s, 1H, NH), 8.2 (s, 1H, NH), 7.61 (d, 1H, $J = 5$, PyH6), 7.28–7.20 (m, 4H, Ph), 7.0 (d, 1H, $J = 7.5$, PyH4), 6.52 (dd, 1H, $J = 5$, $J = 5$, PyH5), 6.2 (s, 1H, H2), 2.8 (s, 3H, Me), 3.3 (s, 3H, Me); ¹³C NMR, δ (ppm) = 181.2 (C=O), 162.7 (C1), 155.1 (Ph), 145.9 (PyC2), 144.5 (PyC6), 129.6, 129, 127.2 (3C, Ph), 128.2 (PyC4), 122.4 (PyC3), 113.8 (PyC5), 95.1 (CCl₃), 89 (C2), 39.5 (Me), 21.7 (Me). Anal. Calcd. for $C_{23}H_{20}Cl_3N_3O_4S$ (mw 540.85): C 51.08% H 3.73% N 7.77%. Found: C, 50.92; H, 3.58; N, 7.69%.

N³-[1-(4-Methoxyphenyl)-3-oxo-4,4,4-trichlorobut-1-en-1-yl]-N²-(methanesulfonyl)-2,3-diaminopyridine (3i). Yield 66%; mp 180–182°C; ¹H NMR, δ (ppm) = 11.0 (s, 1H, NH), 8.1 (s, 1H, NH), 7.5 (d, 1H, $J = 5$, PyH6), 7.29 (d, 2H, $^3J = 7$, Ph), 7.0 (s, 1H, $J = 7.5$, PyH4), 6.69 (d, 2H, $^3J = 7$, Ph), 6.55 (dd, 1H, $J = 5$, $J = 5$, PyH5), 6.2 (s, 1H, H2), 3.8 (s, 1H, OMe), 2.8 (s, 3H, Me); ¹³C NMR, δ (ppm) = 182.5 (C=O), 164.8 (C1), 152.1 (PyC6), 138.6 (PyC4), 134.9 (PyC2), 134.8, 132.9, 129.4, 128.5, 125.9 (5C, Ph), 124.2 (PyC3), 112.2 (PyC5), 96.3 (CCl3), 93.9 (C2), 53.4 (OMe), 39.4 (Me). Anal. Calcd. for $C_{22}H_{17}Cl_3FN_3O_3S$ (mw 528.81): C, 49.97; H, 3.24; N, 7.95%. Found: C, 50.12; H, 3.27; N, 8.01%.

N³-[1-(4-Bromophenyl)-3-oxo-4,4,4-trichlorobut-1-en-1-yl]-N²-(methanesulfonyl)-2,3-diaminopyridine (3l). Yield 61%; mp 177–179°C; ¹H NMR, δ (ppm) = 11.0 (s, 1H, NH), 7.8 (s, 1H, NH), 7.7 (bs, 1H, PyH6), 7.5 (bs, 2H, Ph), 7.2 (bs, 2H, Ph), 6.9 (bs, 1H, PyH4), 6.5 (bs, 1H, PyH5), 6.1 (s, 1H, H2), 2.8 (s, 3H, Me); ¹³C NMR, δ (ppm) = 182.5 (C=O), 165.2 (C1), 153.1 (PyC6), 141.7 (PyC2), 136.3 (PyC4), 132.5, 132.2, 129.4, 125.6 (4C, Ph), 121.3 (PyC3), 113.3 (PyC5), 96.4 (CCl₃), 92.5 (C2), 52.5 (Me). Anal. Calcd. for $C_{22}H_{17}BrCl_3N_3O_3S$ (mw 589.72): C, 44.81; H, 2.91; N, 7.13%. Found: C, 44.99; H, 3.01; N, 7.19%.

General procedure for the preparation of substituted 2-aryl(heteroaryl)-3H-pyrido[2,3-b][1,4]diazepin-4(5H)-ones (4g-p).

Method A: From N³-[1-aryl(heteroaryl)-3-oxo-4,4,4-trichlorobut-1-en-1-yl]-2,3-diaminopyridines (2g-p). To a stirred solutions of *N³*-[1-aryl(heteroaryl)-3-oxo-4,4,4-trichlorobut-1-en-1-yl]-2,3-diaminopyridines (**2g-p**) (3 mmol) in 5 mL of dry ethanol, were added CH₃ONa (3 mmol). The reactions were

carried out under reflux during 24 h. After the reaction time the solvent was removed under reduced pressure and the crude solid products were washed with water and then with chloroform, obtaining dark solids (**4g-p**), as pure compounds (yields 70–85%).

Method B: From 4-aryl(heteroaryl)-4-methoxy-1,1,1-trichlorobut-3-en-2-ones (1g-p). To a stirred solutions of 2,3-diaminopyridine (2 mmol, 0.218 g), in 6 mL of dry methanol, was added CH₃ONa (2 mmol). After 10 min, the respective 4-aryl(heteroaryl)-4-methoxy-1,1,1-trichlorobut-3-en-2-ones (**1g-p**) were added (2 mmol) in one portion and the solutions were stirred at 60–65°C during 24 h. After the reaction time the solvent was removed under reduced pressure and the crude solid products were washed with water and then with chloroform, obtaining dark solids (**4g-p**), as pure compounds (yields 52–70%).

2-Phenyl-3H-pyrido[2,3-b][1,4]diazepin-4(5H)-one (4g). Yield 52%; mp 250–252°C. See ref. [3] yield 65%; mp 258°C; ¹H NMR, δ (ppm) = 10.9 (s, 1H, NH), 8.3 (d, 1H, $J = 5$, H7), 8.0 (bs, 2H, Ph), 7.8 (bs, 1H, H9), 7.5 (bs, 3H, Ph), 7.3 (bs, 1H, H8), 3.6 (s, 2H, H3); ¹³C NMR, δ (ppm) = 166.1 (C=O), 159.3 (C2), 146 (C7), 142.4 (C5a), 136.7 (Ph), 136.3 (C9a), 134.4 (C9), 131.2 (Ph), 128.7 (Ph), 127.6 (Ph), 120 (C8), 40.2 (C3).

2-(4-Methylphenyl)-3H-pyrido[2,3-b][1,4]diazepin-4(5H)-one (4h). Yield 55%; mp 257–259°C; ¹H NMR, δ (ppm) = 10.8 (s, 1H, NH), 8.3 (d, 1H, $J = 5$, H7), 7.9 (d, $^3J = 7$, 2H, Ph), 7.8 (d, $J = 7$, 1H, H9), 7.35–7.33 (m, 3H, Ph and H8), 3.5 (s, 2H, H3), 2.3 (s, 3H, Me); ¹³C NMR, δ (ppm) = 165.7 (C=O), 158.9 (C2), 145.4 (C7), 142.1 (C5a), 140.9 (Ph), 135.2 (C9), 134.2 (C9a), 133.9 (Ph), 128.9 (Ph), 127.3 (Ph), 119.5 (C8), 20.4 (Me). Anal. Calcd. for $C_{15}H_{13}N_3O$ (mw 251.29): C, 71.70; H 5.21; N 16.72%. Found: C, 71.83; H, 5.31; N, 16.75%.

2-(4-Methoxyphenyl)-3H-pyrido[2,3-b][1,4]diazepin-4(5H)-one (4i). Yield 57%; mp 245–247°C; ¹H NMR, δ (ppm) = 11.0 (s, 1H, NH), 8.4 (d, 1H, $J = 5$, H7), 8.1 (d, $^3J = 8.5$, 2H, Ph), 7.9 (d, $J = 7$, 1H, H9), 7.4 (bs, 1H, H8), 7.1 (d, 2H, $^3J = 8.5$, Ph), 3.9 (s, 2H, OMe), 3.6 (s, 2H, H3); ¹³C NMR, δ (ppm) = 166.0 (C=O), 161.8 (C2), 158.6 (Ph), 145.4 (C7), 142.4 (C5a), 136.1 (Ph), 134.6 (C9a), 129.6 (Ph), 129,1 (C9), 119.9 (C8), 114 (Ph), 55.3 (OMe), 40.6 (C3). Anal. Calcd. for $C_{15}H_{13}N_3O_2$ (mw 267.29): C, 67.41; H, 4.90; N, 15.72%. Found: C, 67.20; H,4.95; N, 15.83%.

2-(4-Fluorophenyl)-3H-pyrido[2,3-b][1,4]diazepin-4(5H)-one (4j). Yield 60%; mp 252–254°C; ¹H NMR, δ (ppm) = 10.9 (d, 1H, NH), 8.3 (d, 1H, $J = 5$, H7), 8.1 (bs, 2H, Ph), 7.8 (bs, 1H, H9), 7.40–7.31 (m, 3H, Ph and H8), 3.6 (s, 2H, H3); ¹³C NMR, δ (ppm) = 165.6 (C=O), 157.9 (C2), 156.5 (d, $^1J_{CF} = 250$, Ph), 145.7 (C7), 142.1 (C5a), 135.8 (d, $^4J_{CF} = 22$, Ph), 134.1 (C9a), 133.2 (C9), 129.9 (d, $^3J_{CF} = 9$, Ph), 119.7 (C8), 115.3 (d, $^2J_{CF} = 22$), 33.9 (C3). Anal. Calcd. for $C_{14}H_{10}FN_3O$ (mw 255.25): C, 65.88; H, 3.95; N 16.46%. Found: C, 66.02; H, 3.80; N, 16.37%.

2-(4-Chlorophenyl)-3H-pyrido[2,3-b][1,4]diazepin-4(5H)-one (4k). Yield 64%; mp 262–264°C; ¹H NMR, δ (ppm) =10.8 (s, 1H, NH), 8.3 (d, 1H, $J = 5$, H7), 8.0 (d, $^3J = 8$, 2H, Ph), 7.8 (d, $J = 7$, 1H, H9), 7.7 (d, $^3J = 8$, 2H, Ph), 7.3 (bs, 1H, H8), 3.5 (s, 2H, H3); ¹³C NMR, δ (ppm) = 165.9 (C=O), 158 (C2), 145.8 (C7), 143 (C5a), 138.3 (C9a), 135.9 (C9), 133.9 (Ph), 131.3 (Ph), 129.2 (Ph), 119.9 (C8). Anal. Calcd.

for $C_{14}H_{10}ClN_3O$ (mw 271.71): C, 61.89; H, 3.71; N, 15.47%. Found: C, 61.94; H, 3.68; N, 15.32%.

2-(4-Bromophenyl)-3*H*-pyrido[2,3-*b*][1,4]-diazepin-4(5*H*)-one (4*l*). Yield 53%; mp 266–268°C; ^{1}H NMR, δ (ppm) =10.6 (s, 1H, NH), 8.3 (d, 1H, *J* = 5, H7), 8.0 (bs, 2H, Ph), 7.8 (bs, 1H, H9), 7.7 (bs, 2H, Ph), 7.3 (bs, 1H, H8), 3.5 (s, 2H, H3); ^{13}C NMR, δ (ppm) = 165.5 (C=O), 158 (C2), 145.8 (C7), 142.1 (C5a), 135.9 (C9), 135.8 (C9a), 133.9, 131.3, 129.1, 124.7 (4C, Ph), 119.6 (C8). Anal. Calcd. for $C_{14}H_{10}BrN_3O$ (mw 316.16): C, 53.19; H, 3.19; N, 13.29%. Found: C, 53.02; H, 3.10; N, 13.17%.

2-(4,4′-Biphenyl)-3*H*-pyrido[2,3-*b*][1,4]-diazepin-4-one (4*m*). Yield 59%; mp 248–250°C; ^{1}H NMR, δ (ppm) =11.0 (s, 1H, NH), 8.3 (d, *J* = 5, 1H, H7), 8.0 (bs, ^3J = 8, 2H, Ph), 7.9–7.8 (m, 2H, Ph and 1H, H9), 7.7 (d, ^3J = 8, 2H, Ph), 7.5 (t, 2H, ^3J = 8, Ph), 7.4 (t, 1H, ^3J = 8, Ph), 7.3 (dd, *J* = 5, *J* = 5, 1H, H8), 3.6 (s, 2H, H3); ^{13}C NMR, δ (ppm) = 165.7 (C=O), 158.6 (C2), 145.6 (C7), 142.5 (C5a), 142.1 (Ph), 138.7 (C9a), 135.9 (C9), 135.5, 134.2, 128.5, 127.9, 127.6, 126.5, 126.4 (7C, Ph), 119.6 (C8). Anal. Calcd. for $C_{20}H_{15}N_3O$ (mw 313.36): C, 76.66; H, 4.82; N 13.41%. Found: C, 76.45; H, 4.71; N, 13.20%.

2-(1-Naphthyl)-3*H*-pyrido[2,3-*b*][1,4]-diazepin-4-one (4*n*). Yield 67%; mp 251–253°C; ^{1}H NMR, δ (ppm) = 8.5 (s, 1H, NH), 8.3 (d, 1H, *J* = 5, H7), 7.9 (bs, 2H, Ph), 7.8 (bs, 2H, Ph), 7.7–7.5 (m, 2H, OH and H9 and 2H, Ph), 7.2 (bs, 1H, Ph), 6.7 (bs, 1H, Ph), 6.3 (bs, 1H, H8), 3.6 (s, 2H, H3); ^{13}C NMR, δ (ppm) = 170.8 (Ph), 166.9 (C=O), 161.2 (C2), 148.5 (C7), 136.1 (C5a), 134.9 (C9), 132.8 (C9a), 131.2 (Ph), 127.7–124.9 (Ph), 113.8 (C8). Anal. Calcd. for $C_{18}H_{13}N_3O$ (mw 287.32): C, 75.25; H, 4.56; N, 14.62%. Found: C, 75.48; H, 4.85; N, 14.83%.

2-(2-Furyl)-3*H*-pyrido[2,3-*b*][1,4]-diazepin-4-one (4*o*). Yield 62%; mp 218–220°C; ^{1}H NMR, δ (ppm) =11.0 (s, 1H, NH), 8.3 (d, 1H, *J* = 5, H7), 8.20–8.18 (m, OH, 1H, fr), 7.8 (bs, 1H, H9), 7.7 (bs, 1H, fr), 7.5 (bs, 1H, fr), 7.4 (bs, 1H, H8), 3.6 (s, 2H, H3); ^{13}C NMR, δ (ppm) = 165.8 (C=O), 154.2 (C2), 145.8 (C7), 143.0 (fr), 136.1 (C9a), 134.1 (C9), 133.2 (fr), 131.6 (fr), 128.4 (fr), 120.1 (C8), 40.3 (C3). Anal. Calcd. for $C_{12}H_9N_3O_2$ (mw 227.22): C, 63.43; H, 3.99; N, 18.49%. Found: C, 63.57; H, 4.03; N, 18.55%.

2-(2-Thienyl)-3*H*-pyrido[2,3-*b*][1,4]-diazepin-4-one (4*p*). Yield 70%; mp 264–266°C; ^{1}H NMR, δ (ppm) =10.9 (s, 1H, NH), 8.3 (d, 1H, *J* = 5, H7), 7.9 (bs, 1H, H9), 7.6 (bs, 1H, tn), 7.4 (bs, 1H, tn), 7.0 (bs, 1H, H8), 6.9 (bs, 1H, tn), 3.6 (s, 2H, H3); ^{13}C NMR, δ (ppm) = 165.8 (C=O), 154.8 (C2), 145.8 (C7), 143 (tn), 142.5 (tn), 136.1 (C9), 134.1 (C9a), 133.2, 131.6, 128.4 (3C, tn), 120.1 (C8). Anal. Calcd. for $C_{12}H_9N_3OS$ (mw 243.28): C, 59.24; H, 3.73; N, 17.27%. Found: C, 59.37; H, 3.80; N, 17.32%.

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[16]　Crystallographic data for compound **2g**, reported in this article, have been deposited with the Cambridge Crystallographic Data Center (CCDC 687399). Copies of the data can be obtained, free of charge, on application to CCDC 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).