Synthesis and Reactions of 4-Hydroxy-8,9,10,11-tetrahydropyrido[3,2,1-*jk*]carbazol-6-ones

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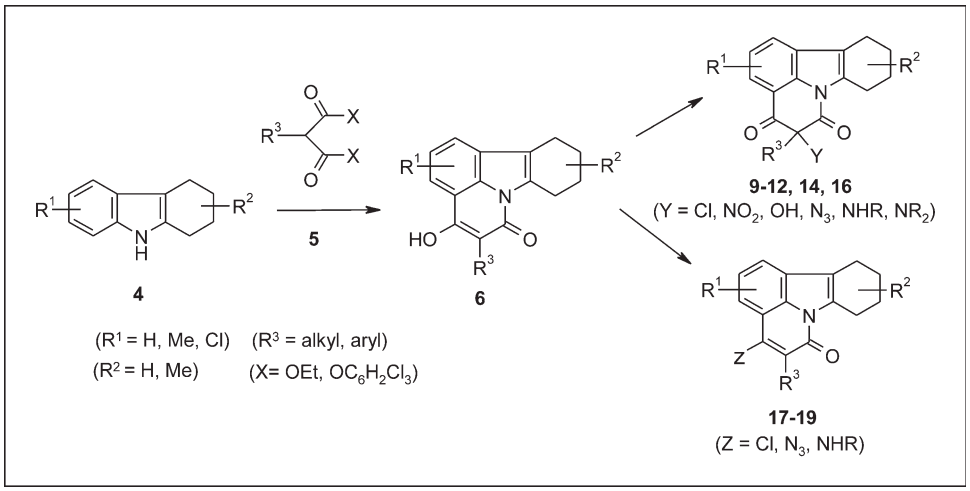

Tetrahydrocarbazoles **4** obtained from phenylhydrazines and cyclohexanones gave by cyclocondensation with 2-substituted malonates **5** in all cases 4-hydroxy-8,9,10,11-tetrahydropyrido[3,2,1-*jk*]carbazol-6-ones **6** by attack at the nitrogen and the aromatic ring of tetrahydrocarbazoles **4**; the direction of the cyclization was not dependent on substituents either in the aromatic or the saturated ring; isomeric pyridocarbazoles could not be isolated. Electrophilic substitutions of pyridocarbazoles **6** under mild conditions took place exclusively at the 5-position and gave pyridocarbazolediones **9**-**11** with 5-nitro-, 5-hydroxy or 5-chloro-substituents. Exchange of the chloro substituent in **11** gave 5-azido- and 5-amino products **12**, **14** or **16**. Reactions at the aromatic ring were not observed. Chlorination of 4-hydroxypyridocarbazoles **6** with phosphoryl chloride by nucleophilic substitution took place exclusively at the 4-position and gave 4-chloropyridocarbazolones **17**, which were further reacted to azides and amines **18, 19**.

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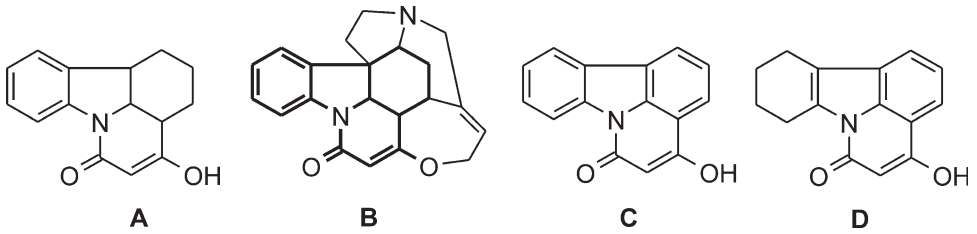
INTRODUCTION

Tetrahydropyrido[3,2,1-*jk*]carbazol-6-one **A** is part of the heterocyclic skeleton of many natural products (*e.g.* strychnos alkaloids such as strychninolones **B** [1] and derivatives such as brucinolones [2] and vomicin [3]). It possesses the biologically interesting combination of an indole and a 2-pyridone structure. Moreover, some derivatives have found interest in pharmacological investigations [4]. Recently, we published the synthesis and reactions of pyrido[3,2,1-*jk*]carbazol-6-ones **C** with two aromatic rings [5]. In this article, we report about the synthesis and reactions of tetrahydropyrido [3,2,1-*jk*]carbazol-6-ones **D** having partial structures more similar to the natural products (Scheme 1).

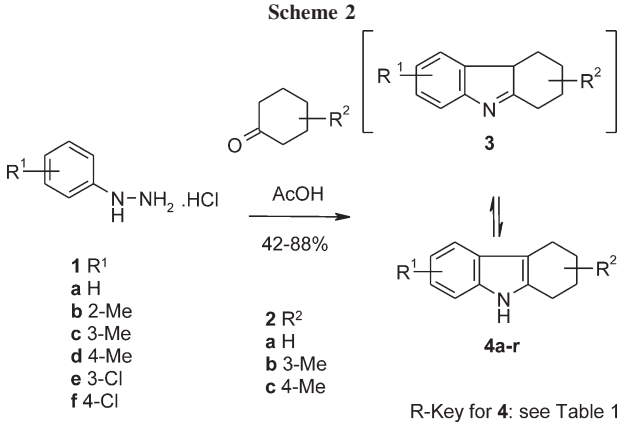
RESULTS AND DISCUSSION

Our approach to the tetrahydro-pyridocarbazole system started with the synthesis of 2,3,4,5-tetrahydro-1*H*-carbazoles **4** with suitable substituents at the desired positions. Despite numerous reactions and catalysts described in the literature, such as the cyclization of cyclohexanone phenylhydrazones [6] or 2-phenylcyclohexanone oxime [7], the reaction of 2-chlorocyclohexanone [8] or 2-hydroxycyclohexanone with aniline [9], or the hydrogenation of carbazole [10], we found that an adapted version of a long-known procedure from Ref. [11] gave the best and simplest approach. Our synthetic approach started from phenylhydrazines **1** and cyclohexanones **2** in acetic acid as solvent without isolation of

Scheme 1



Scheme 2



phenylhydrazones, and we combined this reaction with a one-pot release of chloro- and methyl substituted phenylhydrazines **1**, which are commercially available only as hydrochlorides. The cumbersome release of oily and sensitive free phenylhydrazine bases could be skipped, when sodium acetate was added to the reaction mixture which gave *in situ* the desired phenylhydrazines. Excess sodium acetate and formed sodium chloride was removed at the end of the reaction during work-up by precipitation with diethyl ether.

To study the influence of substituents at the aromatic ring, chloro- and methyl-phenylhydrazines **1** were reacted with cyclohexanones **2** to synthesize a series of

Scheme 3

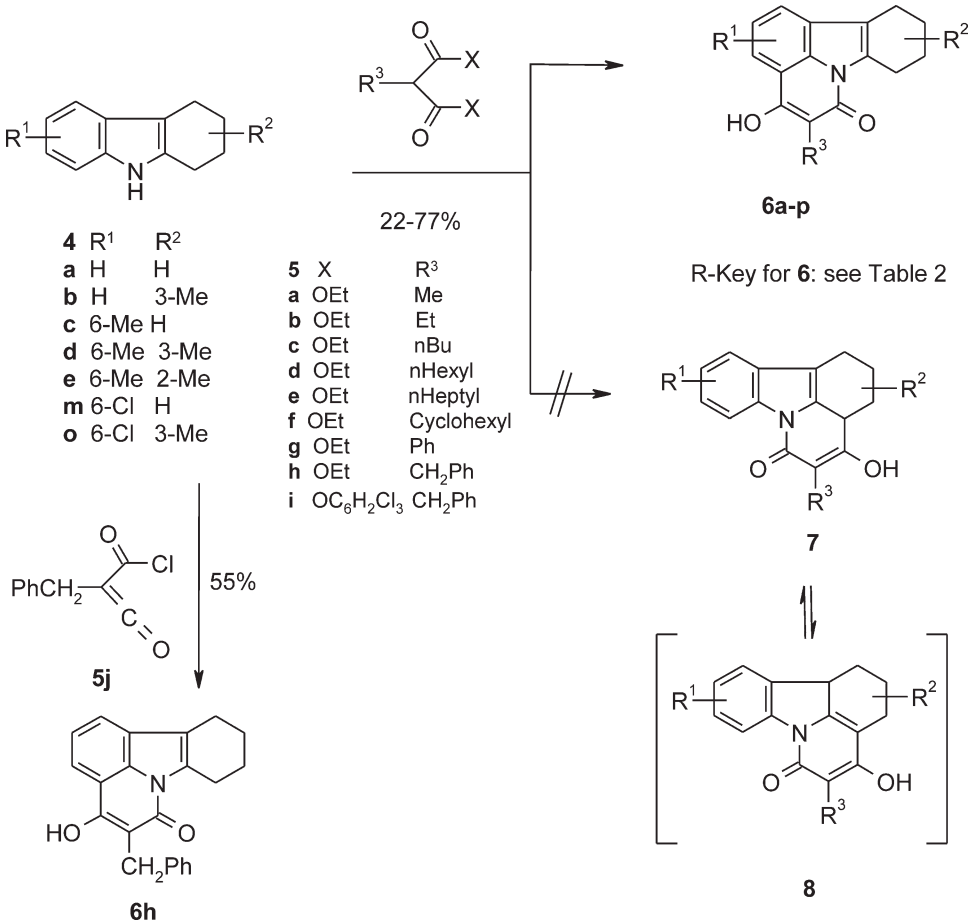


Table 1

2,3,4,9-Tetrahydro-1*H*-carbazoles (**4**).

Compound	R^1	R^2	Chemical name	Method: yield(%) (starting material)	mp (°C) solvent	IR (KBr-discs, cm^{-1})	^1H NMR (DMSO-d_6), δ	Elemental formula (molecular mass), Elemental analysis (calculated/found)
4a	H	H	2,3,4,9-Tetrahydro-1*H*-carbazole	B:88 (**1a**, **2a**)	115–117(ethanol) lit. 116 [11,20,21]			
4b	H	3-Me	3-Methyl-2,3,4,9-tetrahydro-1*H*-carbazole	B:85 (**1a**, **2c**)	109–110 (cyclohexane) lit. 109–110 [22]			
4c	6-Me	H	6-Methyl-2,3,4,9-tetrahydro-1*H*-carbazole	B:80 (**1d**, **2a**)	146 (ethanol) lit. 145–147 [23,24]			
4d	6-Me	3-Me	3,6-Dimethyl-2,3,4,9-tetrahydro-1*H*-carbazole	A:66 (**1d**, **2c**)	113 (ethanol) lit. 112 [20,21]	3395 s, 2951 m, 2915 s, 2863 m, 1588 s	1.07 (d, J = 6.5 Hz, 3 H, 3-Me), 1.37–1.42 (m, 1 H, 3-CH), 1.86–1.89 (m, 2 H, 2-CH_2), 2.26–2.31 (m, 1 H, 4-CH_2), 2.34 (s, 3 H, 6-Me), 2.54–2.58 (m, 1 H, 4-CH_2), 2.63–2.68 and 2.72–2.79 (2 m, 2 H, 1-CH_2), 6.79 (d, J = 8.3 Hz, 1 H, 7-H), 7.09–7.12 (m, 2 H, 5-H, 8-H), 10.43 (s, 1 H, NH)	
4e	6-Me	2-Me	2,6-Dimethyl-2,3,4,9-tetrahydro-1*H*-carbazole	A: 63 (**1d**, **2b**)	147 (ethanol), lit. 137-146 [21,24]	3395 s, 2952 m, 2915 s, 2863 m, 1588 s, 1457 s	1.07 (d, J = 6.5 Hz, 3 H, 2-Me), 1.36–1.46 (m, 1 H, 2-CH), 1.86-1.95 (m, 2 H, 3-CH_2), 2.26–2.30 (m, 1 H, 4-CH_2), 2.34 (s, 3 H, 6-Me), 2.54–2.58 (m, 1 H, 4-CH_2), 2.63-2.68 (m, 1 H, 1-CH2), 2.72–2.78 (m, 1 H, 1-CH_2), 6.78 (d, J = 8.3 Hz, 1 H, 7-H), 7.09–7.11 (m, 2 H, 5-H, 8-H), 10.43 (s, 1 H, NH).	
4f	7-Me	3-Me	3,7-Dimethyl- 2,3,4,9-tetrahydro-1*H*-carbazole	A: 60 (**1c**, **2c**)[a]	98 (ethanol)	3387 s, 2923 s, 1629 m, 1458 m	1.08 (d, J = 6.5 Hz, 3 H, 3-Me), 1.39–1.45 (m, 1 H, 3-CH), 1.84–1.87 (m, 2 H, 2-CH_2), 2.34 (s, 3 H, 7-Me), 2.41–2.45 and 2.53–2.56 (2 m, 2 H, 4-CH_2), 2.67–2.69 and 2.74–2.79 (2 m, 2 H, 1-CH_2), 6.73 (d, J = 8.0 Hz, 1 H, 6-H), 7.50 (s, 1 H, 8-H), 7.19 (d, J = 8.0 Hz, 1 H, 5-H), 10.44 (s, 1 H, NH)	$C_{14}H_{17}N$ (199.30) C 84.37/84.64 H 8.60/8.67 N 7.03/7.38

(*Continued*)

Table 1
(*Continued*)

Compound	R^1	R^2	Chemical name	Method: yield(%) (starting material)	mp (°C) solvent	IR (KBr-discs, cm^{-1})	^1H NMR (DMSO-d_6), δ	Elemental formula (molecular mass), Elemental analysis (calculated/found)
4g	5-Me	3-Me	3,5-Dimethyl- 2,3,4,9-tetrahydro-1*H*-carbazole	A: 5 (**1c**, **2c**)[a]	94 (ethanol)	3386 s, 2921 s, 1565 w, 1457 w	1.08 (d, J = 6.5 Hz, 3 H, 3-Me), 1.42–1.47 (m, Hz, 1 H, 3-CH), 1.87–1.92 (m, 2 H, 2-CH_2), 2.30–2.35 (m, 1 H, 4-CH_2), 2.68 (s, 3 H, 5-CH_3), 2.55–2.59 (m, 1 H, 4-CH_2), 2.60-2.65 and 2.74–2.78 (2 m, 2 H, 1-CH_2), 6.60 (d, J = 7.0 Hz, 1 H, 6-H), 6.82 (t, J = 7.6 Hz, 1 H, 7-H), 7.02 (d, J = 7.0 Hz, 1 H, 8-H), 10.54 (s, 1 H, NH)	$C_{14}H_{17}N$ (199.30) C 84.37/84.72 H 8.60/8.36 N 7.03/6.75
4h	7-Me	2-Me	2,7-Dimethyl-2,3,4,9-tetrahydro-1*H*-carbazole	A: 63 (**1c**, **2b**)[a]	97 (ethanol)	3406s, 3380 s, 2945 m, 2921 s, 1460 w, 1454 w	1.07 (d, J = 6.5 Hz, 3 H, 2-Me), 1.37–1.42 (m, 1 H, 2-CH), 1.85–1.89 (m, 2 H, 3-CH_2), 2.24–2.32 (m, 1 H, 4-CH_2), 2.34 (s, 3 H, 7-Me), 2.53–2.58 (m, 1 H, 4-CH_2), 2.63–2.67 and 2.71–2.77 (2 m, 2 H, 1-CH_2), 6.72 (d, J = 8.0 Hz, 1 H, 6-H), 7.00 (s, 1 H, 8-H), 7.18 (d, J = 8.0 Hz, 1 H, 5-H), 10.41 (s, 1 H, NH)	$C_{14}H_{17}N$ (199.30) C 84.37/84.03 H 8.60/8.24 N 7.03/7.35
4i	5-Me	2-Me	2,5-Dimethyl-2,3,4,9-tetrahydro-1*H*-carbazole	A: 4 (**1c**, **2b**)[a]	95 (ethanol)	3405 s, 3380 s, 2945 m, 2920 s, 2359 m, 1460 w, 1452 m	1.08 (d, J = 6.5 Hz, 3 H, 2-Me), 1.36–1.42 (m, 1 H, 2-CH), 1.85–1.89 (m, 2 H, 3-CH_2), 2.25–2.32 (m, 1 H, 4-CH_2), 2.53 (s, 3 H, 5-Me), 2.56–2.58 (m, 1 H, 4-CH_2), 2.63–2.66 and 2.72–2.77 (2 m, 2 H, 1-CH_2), 6.60 (d, J = 7.0 Hz, 1 H, 6-H), 6.80 (t, J = 7.6 Hz, 1 H, 7-H), 7.02 (d, J = 7.0 Hz, 1 H, 8-H), 10.52 (s, 1 H, NH)	$C_{14}H_{17}N$ (199.30) C 84.37/84.76 H 8.60/8.98 N 7.03/6.66
4j	8-Me	H	8-Methyl-2,3,4,9-tetrahydro-1*H*-carbazole	A: 43 (**1b**, **2a**)	95 (ethanol) lit. 96–98 [23,25]			

(*Continued*)

Table 1
(*Continued*)

Compound	R^1	R^2	Chemical name	Method: yield(%) (starting material)	mp (°C) solvent	IR (KBr-discs, cm^{-1})	^1H NMR (DMSO-d_6), δ	Elemental formula (molecular mass), Elemental analysis (calculated/found)
4k	8-Me	2-Me	2,8-Dimethyl-2,3,4,9-tetrahydro-1*H*-carbazole	A: 46 (**1b**, **2b**)	102 (ethanol) lit. 103 [21,24]	3391 s, 2948 s, 2915 s, 2838 s, 1617 m cm^{-1}	1.09 (d, J = 6.7 Hz, 3 H, 2-Me), 1.36–1.47 (m, 1 H, 2-CH), 1.87–1.94 (m, 2 H, 3-CH_2), 2.29–2.36 (m, 1 H, 4-CH2), 2.40 (s, 3 H, 8-Me), 2.56–2.61 (m, 1 H, 4-CH_2), 2.66–2.70 (m, 1 H, 1-CH_2), 2.77–2.83 (m, 1 H, 1-CH_2), 6.75–6.83 (m, 2 H, 6-H, 7-H), 7.15 (d, J = 7.5 Hz, 1 H, 5-H), 10.48 (s, 1 H, NH)	
4l	8-Me	3-Me	3,8-Dimethyl-2,3,4,9-tetrahydro-1*H*-carbazole	A: 48 (**1b**, **2c**)	106 (ethanol) (lit. 108–109.6 [25])	3432 s, 3279 s, 2946 m, 2915 s, 2832 m, 1618 m	1.19 (s, 3 H, 3-Me), 1.45–1.53 (m, 1 H, 3-CH), 1.88–1.92 (m, 2 H, 2-CH_2), 2.142.21 (m, 1 H, 4-CH_2), 2.40 (s, 3 H, 8-Me), 2.72–2.75 (m, 3 H, 4-CH_2), 2.68–2.70 and 2.81–2.83 (2 m, 2 H, 1-CH_2), 6.75–6.83 (m, 2 H, 6-H, 7-H), 7.14 (d, J = 7.5 Hz, 1 H, 5-H), 10.52 (s, 1 H, NH)	
4m	6-Cl	H	6-Chloro-2,3,4,9-tetrahydro-1*H*-carbazole	B: 81 (**1f**, **2a**)	149 (ethanol) (lit. 142–147 [26]			
4n	6-Cl	2-Me	6-Chloro-2-methyl-2,3,4,9-tetrahydro-1*H*-carbazole	A: 86 (**1f**, **2b**)	142 (ethanol)	3402 s, 2922 s, 1580 m	1.07 (d, J = 6.5 Hz, 3 H, 2-Me), 1.36–1.45 (m, 1 H, 2-CH), 1.85–1.91 (m, 2 H, 3-CH_2), 2.27–2.34 and 2.49–2.57 (2 m, 2 H, 4-CH_2), 2.64–2.68 and 2.75–2.79 (2 m, 2 H, 1-CH_2), 6.84–6.97 (d, J = 8.5 Hz, 1 H, 8-H), 7.24 (d, J = 8.5 Hz, 1 H, 7-H), 7.33 (s, 1 H, 5-H), 10.82 (s, 1 H, NH)	$C_{13}H_{14}ClN$ (219.72) C 71.07/70.76 H 6.42/6.70 N 6.37/6.33 C
4o	6-Cl	3-Me	6-Chloro-3-methyl-2,3,4,9-tetrahydro-1*H*-carbazole	A: 84 (**1f**, **2c**)	115 (ethanol)	3399 s, 2932 m, 2919 m, 2833 m, 1579 m	1.08 (d, J = 6.5 Hz, 3 H, 3-Me), 1.44–1.49 (m, 1 H, 3-CH), 1.87–1.90 (m, 2 H, 2-CH_2), 2.11–2.18 and 2.70–2.75 (2 m, 2 H, 4-CH_2), 6.95 (d, J = 8.5 Hz, 1 H, 8-H), 7.22 (d, J = 8.5 Hz, 1 H, 7-H), 7.32 (s, 1 H, 5-H), 10.85 (s, 1 H, NH)	$C_{13}H_{14}ClN$ (219.72) C 71.07/70.68 H 6.42/6.24 N 6.37/6.19

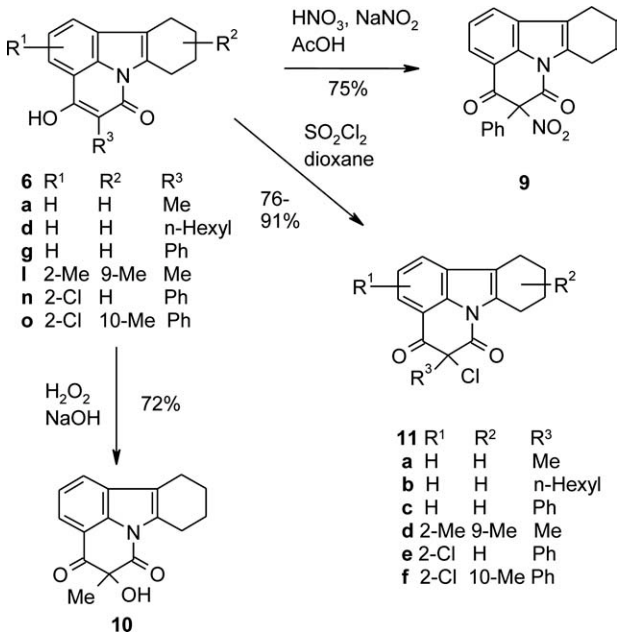
(*Continued*)

Table 1
(*Continued*)

Compound	R^1	R^2	Chemical name	Method: yield(%) (starting material)	mp (°C) solvent	IR (KBr-discs, cm^{-1})	^1H NMR (DMSO-d_6), δ	Elemental formula (molecular mass), Elemental analysis (calculated/found)
4p	7-Cl	H	7-Chloro-2,3,4,9-tetrahydro-1*H*-carbazole	B: 52 (**1e**, **2a**)	160.3 (cyclohexane) lit. 178–180 [27]			
4q	7-Cl	2-Me	7-Chloro-2-methyl-2,3,4,9-tetrahydro-1*H*-carbazole	A: 59 (**1e**, **2b**)	147 (ethanol)	3391 s, 2948 m, 2919 s, 1619 m	1.07 (d, J = 6.5 Hz, 3 H, 2-Me), 1.36–1.45 (m, 1 H, 2-CH), 1.86–1.90 (m, 2 H, 3-CH_2), 2.26–2.33 and 2.55–2.59 (2 m, 2 H, 4-CH_2), 2.65–2.68 and 2.73–2.79 (2 m, 2 H, 1-CH_2), 6.91 (d, J = 8.3 Hz, 1 H, 5-H), 7.24 (s, 1 H, 8-H), 7.31 (d, J = 8.3 Hz, 1 H, 6-H), 10.79 (s, 1 H, NH)	$C_{13}H_{14}ClN$ (219.72) C 71.07/71.03 H 6.42/6.54 N 6.37/6.29.
4r	7-Cl	3-Me	7-Chloro-3-methyl-2,3,4,9-tetrahydro-1*H*-carbazol	A 42 (**1e**, **2c**)	144 (ethanol)	3393 s, 2955 m, 2927 s, 2830 m, 1619 m	1.08 (d, J = 6.5 Hz, 3 H, 3-Me), 1.43–1.51 (m, 1 H, 3-CH), 1.86–190 (m, 2 H, 2-CH_2), 2.08–2.19 and 2.70–2.75 (2 m, 2 H, 4-CH_2, 1-CH_2), 6.91 (d, J = 8.3 Hz, 1 H, 5-H), 7.25 (s, 1 H, 8-H), 7.30 (d, J = 8.3 Hz, 1 H, 6-H), 10.81 (s, 1 H, NH)	$C_{13}H_{14}ClN$ (219.72) C 71.07/70.97 H 6.42/6.44 N 6.37/6.32

[a] The separation of compounds **4f/4g** and **4h/4i** was achieved by dry column flash chromatography (toluene/acetone as gradients).

Scheme 4



tetrahydrocarbazoles with methyl- and chloro substituents in the aromatic ring and methyl substituents in the saturated ring. The structure could be assigned to **4**, as evident from ^{1}H NMR spectra with clear 9-NH signals ranging between 10.4 and 10.8 ppm, and no hydrogen signal of a 4a-proton present in the possibly formed isomeric structure **3**. 2-Methylcyclohexanone (**2**, R^2 = 2-Me) gives, depending on the reaction conditions, a mixture of both isomers of **3** and **4**, 1- or 4a-methyl-tetrahydrocarbazole [12]; the work on these topics is in progress [13]. 3-Methylcyclohexanone (**2b**) gave 2-methyl-tetrahydrocarbazoles **4e, h, i, k, n, q**, as evident from the ^{1}H NMR signal of 4-CH_2 at ~2.6 ppm and of the 2-CH at ~1.4 ppm; the corresponding 4-methyl isomer could not be isolated. From 3-methylphenylhydrazine (**1c**) we isolated both isomers, 7-methyl-tetrahydrocarbazoles **4f,h** and 5-methyl derivatives **4g,i** in a ratio of about 10:1 (Scheme 2).

The cyclocondensation reaction of **4** was performed with ethyl 2-alkyl- and 2-phenylmalonates **5a-h**. ^{1}H NMR spectral data revealed that in all cases the ring closure was directed to the aromatic ring to produce 4-hydroxy-8,9,10,11-tetrahydropyrido[3,2,1-*jk*]carbazol-6-ones **6** as evident from the ratio of aromatic: aliphatic protons and unaffected CH_2 groups in position 8. 6-Chloro-tetrahydrocarbazoles **4m-o** did not show significant influence on the synthesis and gave 2-chloro-pyridocarbazoles **6n-p**. 7-Chloro-tetrahydrocarbazoles **4p-r** gave, probably by deactivation of the aromatic nucleus, very low yields or unseparable mixtures which did not allow the isolation of pure 3-chloro-pyridocarbazoles **6**; the isolation of possibly formed isomers **7/8** was not achieved.

6-Methyl-tetrahydrocarbazoles **4c-e** formed in reasonable yields 2-methyl-pyridocarbazoles **6k-m**. 8-Methyl-tetrahydrocarbazoles **4j-l** prevented the formation of pyridocarbazoles **6** by steric hindrance, but gave again no reaction to isomeric pyridocarbazoles **7/8**.

The yields of pyridocarbazoles **6a-j** without substituents in the aromatic carbazole nucleus were ranging from 20 to 80%. The cyclization reaction proceeds in two steps via an initial malono-monoamide followed by formation of a thermally produced ketene derivative which cyclizes in an electrophilic substitution towards the aromatic carbazole ring [14]. The differing yields can be explained by both a competing malono-diamide formation and side-reactions during the ketene reaction.

There are some other reaction sequences known using highly reactive malonic acid derivatives, which avoid the high temperatures of the second ketene forming step: one of these derivatives is the well established *bis*(2,4,6-trichlorophenyl) malonate (active malonate, magic malonate) [15], another one is (chlorocarbonyl)ethylketene (chlorocarbonylketene, in older literature also named as malonyldichloride) [16]. We compared the reactions of *bis*(2,4,6-trichlorophenyl) 2-benzylmalonate (**5i**) and 2-benzyl-2-(chlorocarbonyl)ethylketene (**5j**) with tetrahydrocarbazole **4a** to 5-benzyl-4-hydroxy-8,9,10,11-tetrahydropyrido[3,2,1:*jk*]carbazol-6-one (**6h**). Both reactions gave the desired product **6h**, trichlorophenylester **5i** in 30% and chlorocarbonylketene **5j** in 55% yield, which is better than the yield of the thermal method, but does not counterbalance the disadvantages of time-consuming and expensive syntheses of **5i** and **5j** (Scheme 3; Table 1).

Tetrahydro-pyridocarbazoles **6** possess besides the biologically interesting indole structure a 4-hydroxy-pyridone structure element, which is susceptible for many reactions. It can exist in tautomeric structures: the 4-hydroxy-6-oxo-structure as drawn in **6** is the predominant structure as evident in all spectroscopic investigations (*e.g.* shown by the hydroxy signal at 10.6–10.9 ppm in the ^{1}H NMR spectra, and a single IR signal for the amide-CO at position 6 at about 1650 cm^{-1}). A reversed 4-oxo-6-hydroxy structure can be excluded because of its missing 4-pyridone signal in IR spectra [17]. However, during reactions with suitable reagents, the molecule can react from its 4,6-dioxo tautomer giving fixed dioxo-derivatives. The carbon at position 5 behaves due to the neighborship of two carbonyl groups as reactive CH acidic moiety, and electrophilic reactions such as nitration are directed first to this position. Therefore, it is possible to nitrate **6a** in position 5 by a gentle reaction with concentrated nitric acid in the presence of sodium nitrite as catalyst in glacial acetic acid already

Table 2

4-Hydroxy-8,9,10,11-tetrahydropyrido[3,2,1-*jk*]carbazol-6-ones (**6**).

Compound	R^1	R^2	R^3	Chemical name	Method: yield(%) (starting material)	mp (°C) solvent	IR (KBr-discs, cm^{-1})	^1H NMR (DMSO-d_6 unless otherwise stated), δ	Elemental formula (molecular mass), elemental analysis (calculated./ found)
6a	H	H	Me	4-Hydroxy-5-methyl-8,9,10,11-tetrahydropyrido [3,2,1-*jk*]carbazol- 6-one	B: 77 (**4a**, **5a**)	144 (ethanol)	3435 s, 2934 s, 1649 m (6-C=O), 1610 s, 1591 w	1.76–1.79 and 1.84–1.86 (2 m, 4 H, 9-CH_2, 10-CH_2), 2.03 (s, 3 H, 5-CH_3), 2.67 (t, J = 7.1 Hz, 2 H, 8-CH_2), 3.08 (t, J = 7.1 Hz, 2 H, 11-CH_2), 7.39 (t, J = 7.7 Hz, 1 H, 2-H), 7.66 (d, J = 7.5 Hz, 1 H, 1-H), 7.85 (d, J = 7.7 Hz, 1 H, 3-H), 10.69 (s, 1 H, OH)	$C_{16}H_{15}NO_2$ (253.30) C 75.87/75.59 H 5.97/5.91 N 5.53/5.57
6b	H	H	Et	5-Ethyl-4-hydroxy-8,9,10,11-tetrahydro-pyrido [3,2,1-*jk*] carbazol-6-one	B: 46 (**4a**, **5b**)	232 (ethanol)	3440 s, 2930 s, 1650 m (6-C=O), 1610 s, 1590 w	0.95 (s, 3 H, Me), 1.75-1.80 and 1.83–1.90 (2 m, 4 H, 9-CH_2, 10-CH_2), 2.58 (q, 2 H, 5-CH_2), 2.65 (t, J = 7.1 Hz, 2 H, 8-CH_2), 3.10 (t, J = 7.1 Hz, 2 H, 11-CH_2), 7.40 (t, J = 7.7 Hz, 1 H, 2-H), 7.65 (d, J = 7.5 Hz, 1 H, 1-H), 7.85 (d, J = 7.7 Hz, 1 H, 3-H), 10.70 (s, 1 H, OH)	$C_{17}H_{17}NO_2$ (267.33) C 76.38/75.92 H 6.41/6.40 N 5.24/5.10
6c	H	H	n-Bu	5-Butyl-4-hydroxy-8,9,10,11-tetrahydro-pyrido [3,2,1-*jk*] carbazol-6-one	B: 37 (**4a**, **5c**)	210 (ethanol)	3400–3350 b, m, 2960 m, 1640 s (6-C=O), 1615 m, 1595 m	0.91 (t, J = 7.0 Hz, 3 H, Me), 1.32–1.42 (m, 2 H, CH_2), 1.47–1.51 (m, 2 H, CH_2), 1.75–1.79 and 1.84–1.90 (2 m, 4 H, 9-CH_2, 10-CH_2), 2.69 (t, J = 7.0 Hz, 5-CH_2), 7.42 (t, J = 7.7 Hz, 1 H, 2-H), 7.66 (d, J = 7.5 Hz, 1 H, 1-H), 7.84 (d, J = 7.7 Hz, 1 H, 3-H), 10.80 (s, 1 H, OH)	$C_{19}H_{21}NO_2$ (295.38): C 77.26/77.54 H 7.17/6.82 N 4.74/4.35

(*Continued*)

Table 2
(*Continued*)

Compound	R^1	R^2	R^3	Chemical name	Method: yield(%) (starting material)	mp (°C) solvent	IR (KBr-discs, cm^{-1})	^1H NMR (DMSO-d_6 unless otherwise stated), δ	Elemental formula (molecular mass), elemental analysis (calculated./ found)
6d	H	H	n-Hexyl	5-Hexyl-4-hydroxy-8,9,10,11-tetrahydropyrido[3,2,1-*jk*]carbazol- 6-one	A: 30 (**4a**, **5d**)	162 (ethanol)	3300-3100 b, 2930 m, 1645 m (6-C=O), 1605 s, 1590 s	0.85 (t, J = 7.0 Hz, 3 H, CH_3), 1.20-1.60 (m, 4 H, 2 hexyl-CH_2), 1.70–1.90 (m, 4 H, 9-CH_2 and 10-CH_2), 2.50-2.70 (m, 4 H, 4-CH_2, 11-CH_2), 3.10 (t, J = 7.0 Hz, 2 H, 8-CH_2), 7.40 (t, J = 7.1 Hz, 1 H, 2-H), 7.65 (d, J = 7.1 Hz, 1 H, 1-H), 7.90 (d, J = 7.1 Hz, 1 H, 3-H), 10.60 (s, OH)	$C_{21}H_{25}NO_2$ (323.44): C 77.99/77.87 H 7.79/7.73 N 4.33/4.46
6e	H	H	n-Heptyl	5-Heptyl-4-hydroxy-8,9,10,11-tetrahydropyrido[3,2,1-*jk*]carbazol-6-one	A: 37 (**4a**, **5e**)	144 (toluene)	3300-3000 b, 2920 s, 1650 m (6-C=O), 1610 s, 1590 s	0.80 (t, J = 7.0 Hz, 3 H, Me), 1.15–1.60 (m, 5 heptyl-CH_2), 1.80–2.00 (m, 4 H, 9-CH_2 and 10-CH_2), 2.50-2.80 (m, 4 H, 4-CH_2, 11-CH_2), 3.10 (t, J = 7.0 Hz, 2 H, 8-CH_2), 7.40 (t, J = 7.1 Hz, 1 H, 2-H), 7.70 (d, J = 7.1 Hz, 1 H, 1-H), 7.90 (d, J = 7 Hz, 1 H, 3-H), 10.65 (s, 1 H, NH)	$C_{22}H_{27}NO_2$ (337.47): C 78.30/78.68 H 8.06/7.78 N 4.15/4.02.
6f	H	H	Cyclohexyl	5-Cyclohexyl-4-hydroxy-8,9,10,11-tetrahydropyrido[3,2,1-*jk*] carbazol-6-one	A: 22 (**4a**, **5f**)	245 (ethanol)	3300–3100 b, 2920m, 1740 w, 1660 s (6-C=O), 1600 s, 1590 sh	1.10–1.50 (m, 4 H, 2 CH_2), 1.60–2.10 (m, 10 H, 5 CH_2), 2.15–2.20 (m, 1 H, CH), 2.60–2.80 (m, 1 H, 8-CH_2), 3.10 (t, J = 7.0 Hz, 11-CH_2), 7.45 (t, J = 7.1 Hz, 1 H, 2-H), 7.70 (d, J = 7.1 Hz, 1 H, 1-H), 8.04 (d, J = 7 Hz, 1 H, 3-H), 10.65 (s, 1 H, NH)	$C_{21}H_{23}NO_2$ (321.42) C 78.47/68.69 H 7.21/ 5.80 N 4.36/ 4.34.
6g	H	H	Ph	4-Hydroxy-5-phenyl-8,9,10,11-tetrahydropyrido[3,2,1-*jk*]carbazol-6-one	B: 37 (**4a**, **5g**)	207 (ethanol); lit 210°C [28,29]			

(*Continued*)

Table 2
(*Continued*)

Compound	R^1	R^2	R^3	Chemical name	Method: yield(%) (starting material)	mp (°C) solvent	IR (KBr-discs, cm^{-1})	^1H NMR (DMSO-d_6 unless otherwise stated), δ	Elemental formula (molecular mass), elemental analysis (calculated./ found)
6h	H	H	CH_2Ph	5-Benzyl-4-hydroxy-8,9,10,11-tetrahydropyrido [3,2,1-*jk*]carbazol-6-one	B: 27 (**4a**, **5h**) Methods C and D:[b]	240 (glacial acetic acid/ water) lit. 240–245 [28]			
6i	H	10-Me	Et	5-Ethyl-4-hydroxy- 10-methyl-8,9,10,11-tetrahydropyrido [3,2,1-*jk*] carbazol-6-one	A: 26 (**4b**, **5b**)	240 (ethanol)	3400–3200 m, 2960 m, 2920 m, 1650 m (6-C=O), 1610 s	1.05 (t, J = 7.0 Hz, Me), 1.4–1.6 and 1.7–2.0 (2 m, 4 H, 9-CH_2, 10-CH_2), 2.20 (t, J = 7.0 Hz, 2 H, 11-CH_2), 2.60 (q, J = 7.0 Hz, 2 H, 5-CH_2), 2.95 (t, J = 7.0 Hz, 2 H, 8-CH_2), 7.35 (t, J = 6.8 Hz, 1 H, 2-H), 7.6 (d, J = 6.8 Hz, 1 H, 1-H), 7.90 (d, J = 6.8 Hz, 1 H, 3-H), 10.70 (s, 1 H, OH)	$C_{18}H_{19}NO_2$ (281.36): C 76.84/76.72 H 6.81/6.72 N 4.98/ 4.83
6j	H	10-Me	n-Bu	5-Butyl-4-hydroxy-10-methyl-8,9,10,11-tetrahydropyrido [3,2,1-*jk*] carbazol-6-one	A: 62 (**4b**, **5c**)	220 (ethanol)	3400–3200 m, 2930 m, 1645 m (6-C=O), 1620 sh, 1600 s	0.80 (t, J = 7.0 Hz, 3 H, butyl-Me), 1.05 (d, J = 7.0 Hz, 3 H, 10-Me), 1.20-1.70 (m, 6 H, 3 CH_2), 1.80–2.00 (m, 2 H, 10-H), 2.20, (t, J = 7.0 Hz, 5-CH_2), 2.55 (t, J = 7 Hz, 2 H, 11-CH_2), 2.95 (t, J = 7 Hz, 2 H, 8-CH_2), 7.35 (t, J = 6.9 Hz, 1 H, 2-H), 7.65 (d, J = 6.9 Jz, 1 H, 1-H), 7.85 (d, J = 6.9 Hz, 1 H, 3-H), 10.90 (s, 1 H, OH)	$C_{20}H_{23}NO_2$ (309.41): C 77.64/77.98 H 7.49/7.21 N 4.53/4.17
6k	2-Me	H	Ph	4-Hydroxy-2-methyl-5-phenyl-8,9,10,11-tetrahydropyrido [3,2,1-*jk*] carbazol-6-one	A: 52 (**4c**, **5g**)	181 (ethanol)	3450 s, 2950 s, 1650 s (6-C=O), 1610 m	1.75–2.00 (m, 4 H, 9-CH_2 and 10-CH_2), 2.65 (s, 3 H, 2 Me)2.75 (t, J = 7.0 Hz, 8-CH_2), 3.10 (t, J = 7.0 Hz, 11-CH_2), 7.25–7.50 (m, 6 H, ArH), 7.80 (s, 1-H), 8.05 (s, 1 H, 3-H), 10.85 (s, OH)	$C_{22}H_{19}NO_2$ -329.4 C 80.22/80.54 H 5.81/5.59 N 4.25/3.89

(*Continued*)

Table 2
(*Continued*)

Compound	R^1	R^2	R^3	Chemical name	Method: yield(%) (starting material)	mp (°C) solvent	IR (KBr-discs, cm^{-1})	^1H NMR (DMSO-d_6 unless otherwise stated), δ	Elemental formula (molecular mass), elemental analysis (calculated./ found)
6l	2-Me	9-Me	Me	4-Hydroxy-2,5,9-trimethyl-8,9,10,11-tetrahydropyrido [3,2,1-*jk*] carbazol-6-one	B: 63 (**4e**, **5a**)	262 (ethanol)	3435 s, 2922 m, 1649 m (6-C=O), 1627 m, 1613 m	1.11 (d, J = 7.0 Hz, 3 H, 9-Me), 1.42–1.47 (m, 1 H, 9-H), 1.87–1.92 (m, 2 H, 10-CH_2), 2.03 (s, 3 H, 5-Me), 2.08 (s, 3 H, 2-Me), 2.56-2.73 (m, 4 H, 8-CH_2, 11-CH_2), 7.50 (d, J = 7.0 Hz, 1 H, 1-H), 7.67 (d, J = 7.0 Hz, 1 H, 3-H), 10.70 (s, 1 H, OH)	$C_{18}H_{19}NO_2$ (281.36) C 76.84/76.49 H 6.81/6.64 N 4.98/4,89
6m	2-Me	10-Me	Ph	4-Hydroxy-2,10-dimethyl-5-phenyl-8,9,10,11-tetrahydropyrido [3,2,1-*jk*]carbazol-6-one	A 49 (**4d**, **5g**)	217 (toluene)	3450 s, 2920 s, 1650 s (6-C=O), 1605 m	1.10 (d, J = 7.0 Hz, 3 H, 10-Me), 1.45–1.50 (m, 1 H, 9-H), 1.85–1.95 (m, 2 H, 9-CH_2), 2.05 (s, 3 H, 2-Me), 2.55-2.75 (m, 4 H, 8-CH_2, 11-CH_2), 7.20–7.70 (m, 5 Ph-H), 7.80 (d, J = 2 Hz, 1 H, 1-H), 8.00 (d, J = 7.0 Hz, 1 H, 3-H), 10.80 (s, 1 H, OH)	$C_{23}H_{21}NO_2$ (343.43) C 80.44/80.28 H 6.16/5.69 N 4.08/4.03
6n	2-Cl	H	Ph	2-Chloro-4-hydroxy- 5-phenyl-8,9,10,11-tetrahydropyrido [3,2,1-*jk*] carbazol-6-one	A: 23 (**4m, 5g**)	200 (ethanol)	3500–3000 m, 2940 m, 1650 m (6-C=O), 1620 s, 1590 sh	1.75–1.95 (m, 4 H, 9-CH_2, 10-CH_2), 2.75 and 3.10 (2 t, J = 7.0 Hz, 11-CH_2 and 8-CH_2), 7.20–7.70 (m, 5 Ph-H), 7.80 (d, J = 2.0 Hz, 1 H, 1-H), 8.00 (d, J = 7.0 Hz, 1 H, 3-H), 11.00 (s, 1 H, OH)	$C_{21}H_{16}ClNO_2$ (349.82): C 72.10/72.45 H 4.61/4.52 N 4.00/3.73
6o	2-Cl	10-Me	Ph	2-Chloro-4-hydroxy-10-methyl-5-phenyl-8,9,10,11-tetrahydro-pyrido [3,2,1-jk]carbazol-6-one	A: 31 (**4o**, **5g**)	268 (toluene)	3200–2800 w, 1650 m (6-C=O), 1625 s, 1595 m	1.05 (d, J = 7.0 Hz, 3 H, 10-Me), 1.30–1.55 (m, 1 H, 10-H), 1.75–2.00 (m, 2 H, 9-CH_2), 2.65 (d, J = 7.0 Hz, 2 H, 11-CH_2), 2.90–3.05 (m, 2 H, 8-CH_2), 7.10–7.60 (m, 5 H, PhH), 7.7 (d, J = 1.5 Hz, 1 H, 1-H), 7.95 (d, J = 1.5 Hz, 1 H, 3-H)	$C_{22}H_{18}ClNO_2$ (363.85): C 72.63/73.01 H 4.99/5.05 N 3.85/3.70

(*Continued*)

Table 2
(*Continued*)

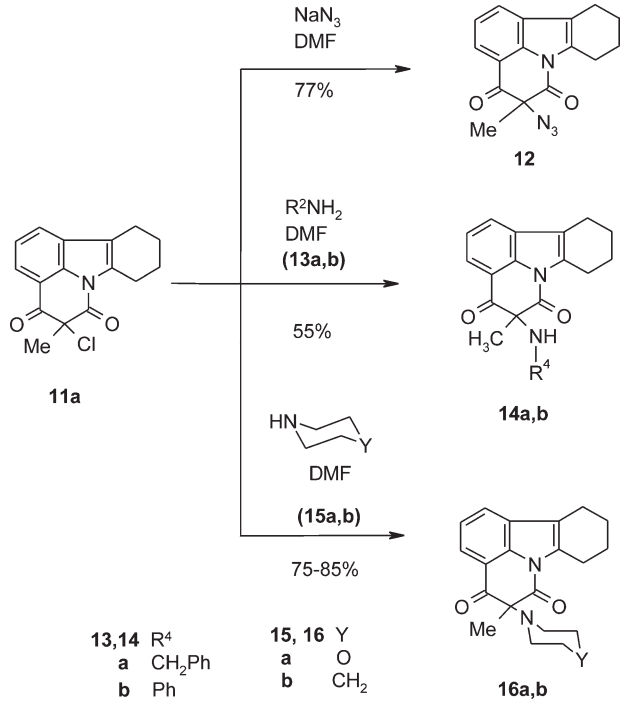
Compound	R^1	R^2	R^3	Chemical name	Method: yield(%) (starting material)	mp (°C) solvent	IR (KBr-discs, cm^{-1})	^1H NMR (DMSO-d_6 unless otherwise stated), δ	Elemental formula (molecular mass), elemental analysis (calculated./ found)
6p	2-Cl	10-Me	Me	2-Chloro-5,10-dimethyl-4-Hydroxy-8,9,10,11- tetrahydropyrido [3,2,1-*jk*]carbazol-6-one	B 66 (**4o**, **5a**)	275 (ethanol)	3432 s, 2919 m, 1649 m (6-C=O), 1624 s, 1561 s	1.07 (d, J = 6.0 Hz, 3 H, 10-Me), 1.44–1.46 (m, 1 H, 10-H), 1.85–1.93 (m, 2 H, 9-CH_2), 2.00 (s, 3 H, 5-H), 2.11–2.18 and 2.73–2.76 (2 m, 2 H, 11-CH_2), 2.88– 2.93 and 3.15–3.20 (2 m, 2 H, 8-CH_2), 7.63 (s, 1 H, 5-H), 7.79 (s, 1 H, 7-H), 10.81 (s, 1 H, OH)	$C_{17}H_{16}ClNO_2$ (301.78): C 67.66/67.76 H 5.34/4.97 N 4.64/4.26

[b]Methods C and D for 6h are described in the experimental part.

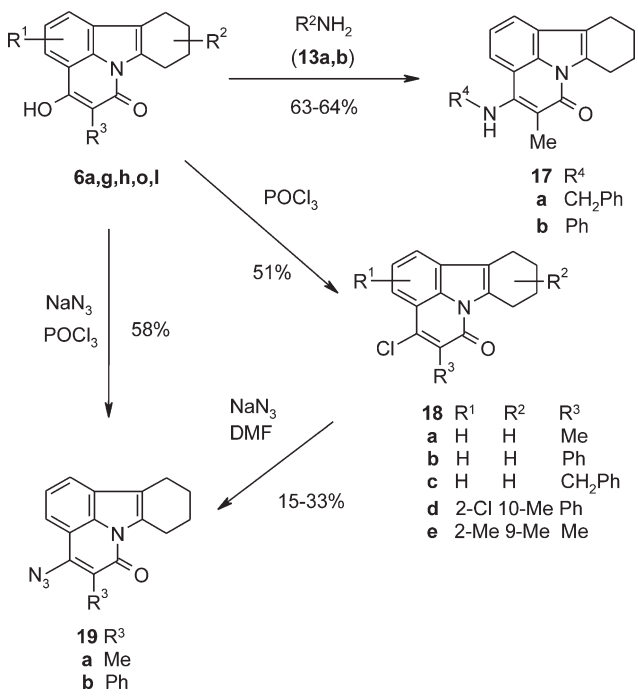
at room temperature. All other aromatic positions (1,2, and 3) remain unaffected, and 5-nitro-pyridocarbazoledione **9** is obtained in 75% yield. Hydroxylation of **6a** with hydrogenperoxide in buffered slightly alkaline aqueous solution gives in good yields 5-hydroxy-pyridocarbazoledione **10**, which contains the 3-hydroxy-2,4-dioxoquinoline structure element present in contents of some *Pseudomonas* bacteria (Scheme 4; Table 2) [18].

Electrophilic chlorination of **6** in position 5 could be performed with sulfuryl chloride. Because of the reactivity of this reagent, 2,5-dimethyl- and 2,5,9-trimethyl derivatives **6a** and **6k** had to be brought to reaction at room temperature, otherwise polychlorinated by-products were formed. The formed 5-chloro-pyridocarbazolediones **11**, which were obtained in excellent yields, serve as starting material for further substitution reactions: as examples an azidation and aminations are shown. The azidation of **11a** proceeds by simple halogen exchange at the aliphatic C-5 position at 50°C and gives in excellent yields 5-azido-pyridocarbazoledione **12**. Amination was performed with primary and secondary amines: **11a** gave with benzylamine (**13a**) the corresponding 5-benzylamino-pyridocarbazoledione **14a** in excellent yields; with aniline (**13b**) as the amino component, the yield of the corresponding 5-phenylamino-pyridocarbazoledione **14b** was slightly lower. Reaction of **1a** with secondary amines such as morpholine (**15a**) or piperidine (**15b**) gave in excellent yields 5-morpholino- and 5-piperidino-pyridocarbazolediones **16a**,**b** (Scheme 5).

Scheme 5



Scheme 6



In contrast to the electrophilic reactions shown above, a nucleophilic displacement takes place at the 4-position of the pyridocarbazolone. The 4-hydroxy group of **6** can be easily displaced by a chloro function, using phosphoryl chloride as reagent, or by substituted amino groups. Amination of **6a** at position 4 can be achieved by reaction of the reactive 4-hydroxy group with benzylamine (**13a**) and gives 4-benzylamino-pyridocarbazolones **17a** in excellent yield. The amination of **6a** with aniline (**13b**) needed the addition of aniline hydrochloride as acidic catalyst and gave in exellent yields 4-anilinopyridocarbazolone **17b**. Chlorination with phosphoryl chloride gave 4-chloropyridocarbazolones **18** in moderate to excellent yields. The nucleophilic exchange of the chloro substituent in 4-chloro-5-methylpyridocarbazolone **18a** against the azide group gave 4-azidopyrido[3,2,1-*jk*]carbazolones **19a** in only 15% yield. 4-Chloro-5-phenylpyridocarbazolone **18b** gave slightly better yields of 33% of the corresponding 4-azidopyrido[3,2,1-*jk*]carbazolone **19b**. To improve the yield, we used our recently developed one-pot synthesis [5] starting from 4-hydroxypyridocarbazolone **6a**, which reacted with a mixture of sodium azide and phosphoryl chloride (probably via reactive phosphoric esters) in dimethylformamide to obtain in this one-pot reaction **19a** in 58% yield (Scheme 6).

CONCLUSION

Our results show that cyclization reactions of 2,3,4,5-tetrahydro-1*H*-carbazoles **1** with malonic acid derivatives give solely the 8,9,10,11-pyrido[3,2,1-*jk*]carbazole system **6**. Attempts to force a cyclization to 1,2,3,3a-tetrahydro-pyrido[3,2,1-jk]carbazole or its tautomeric ring system (**7/8**) by deactivation of the aromatic nucleus by electronic or steric influences failed. Electrophilic and nucleophilic substitution reactions with suitable reagents and conditions took place exclusively at the fused pyridone ring at position 5 or 4, respectively.

EXPERIMENTAL

General. Melting points were determined using a Stuart SMP3 Melting Point Apparatus in open capillary tubes. IR spectra were recorded using a Mattson Galaxy Series FTIR 7020 instrument with potassium bromide discs. NMR spectra were recorded on a Bruker AMX 360 instrument (360 MHz ^{1}H, 90 MHz ^{13}C) or on a Bruker Avance DRX 500 instrument (500 MHz ^{1}H, 125 MHz ^{13}C). Chemical shifts are given in ppm (δ) from the internal TMS standard. Elemental analyses were performed at the Microanalytical Laboratory of the University of Vienna, Austria. Mass spectra were obtained from a HP 1100 LC/MSD mass spectral instrument (positive or negative APCI ion source, 50–200 V, nitrogen). Dry column flash chromatography [19] was carried out on Merck Kieselgel 60 H (5–40 μm). All reactions were monitored by thin layer chromatography on 0.2 mm silica gel F 254 (Merck, Darmstadt, Germany) plates using UV light (254 and 366 nm) for detection. Analytical HPLC was performed on a Shimadzu LC 20 system equipped with a diode array detector (215 and 254 nm) on a Pathfinder AS reversed phase (4.6150 mm, 5 μm) column, running an acetonitrile/water gradient (30–100% acetonitrile). Common reagent-grade chemicals are either commercially available and were used without further purification or prepared by standard literature procedures.

General methods for the Fischer indole synthesis of 2,3,4,9-tetrahydro-1H-carbazoles (4). *Method A (one pot procedure).* To a mixture of anhydrous sodium acetate (2.46 g, 30 mmol) in glacial acetic acid (40 mL) the appropriate cyclohexanone **2** (30 mmol) was added at 90°C, then the corresponding phenylhydrazine hydrochloride **1.HCl** (25 mmol) was added in small portions during 1 h. The reaction mixture was further heated under reflux for 1 h, cooled to room temperature and diluted with diethyl ether (100 mL). The precipitated solid (inorganic salts) was separated by suction filtration and washed with diethyl ether. The combined filtrates were taken to dryness in vacuo, the residue diluted with a mixture of ethanol/water (7:3, 100 mL) and after standing for 3 h, the precipitated product isolated by suction filtration. The product was dried in vacuo at room temperature, then recrystallized from the appropriate solvent using charcoal.

Method B (2-step procedure). The corresponding phenylhydrazine hydrochloride **1.HCl** (27 mmol) was suspended in 0.5*M* aqueous sodium hydroxide (100 mL) and stirred at 70°C for 30 min. After cooling the precipitated oil was separated (loss ~5–10%) and added without further purification to a solution of the appropriate cyclohexanone **2** (30 mmol) in glacial acetic acid (70 mL) in small portions during 1 h. The reaction mixture was then heated under reflux for 1 h and cooled to room temperature under stirring until a solid precipitated. The

mixture was cooled to 5°C, the precipitated solid isolated by suction filtration and the filtrate cooled again to isolate a second crop. The combined solids were washed with water (100 mL) and ethanol/water (7:3, 100 mL), air-dried and then recrystallized from the appropriate solvent using charcoal.

R-key and data of **4a-r**: Table 1.

General Methods for the cyclization of tetrahydrocarbazoles 4 to 4-hydroxy-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazol-6-ones (6). *Method A (thermal neat method).* A mixture of the appropriate diethyl malonate **5** (30 mmol) and the corresponding tetrahydrocarbazole **4** (25 mmol) was heated for 2–3 h to 280–300°C in a metal bath using a Vigreux column equipped with a distillation bridge. During this time the first equivalent of ethanol (25 mmol, about 0.9 mL) was liberated. When the liberation of ethanol had stopped, the reaction mixture was heated for about 30 min to a bath temperature of 330–350°C; during this time the second equivalent of ethanol (0.9 mL, 25 mmol) was liberated. The reaction mixture was cooled to about 80°C, methanol (30 mL) was added, the mixture cooled to room temperature and filtered by suction. The solid was taken up in aqueous sodium hydroxide solution (0.25*M*, 100 mL) and extracted with toluene (100 mL). The aqueous layer was decolorized with charcoal at 50 to 80°C and filtered. Concentrated hydrochloric acid was added to the filtrate until pH ~3, the precipitate filtered by suction, washed acid-free with water, dried and recrystallized from the appropriate solvent.

Method B (thermal solution method). A solution of the appropriate diethyl malonate **5** (30 mmol) and the corresponding tetrahydrocarbazole **4** (25 mmol) in diphenylether (25 mL) was heated under reflux at 250°C in a metal bath using a Vigreux column equipped with a distillation bridge for about 12 h. During this time, 2 equivalents of ethanol were liberated (50 mmol, about 1.8 mL). After cooling to room temperature, diethyl ether (50 mL) was added, and the solid which precipitated was filtered by suction, washed with diethyl ether and dried. The collected solid was taken up in aqueous sodium hydroxide solution (0.25*M*, 100 mL) and filtered by suction. Concentrated hydrochloric acid was added to the filtrate until pH ~3, the precipitate filtered by suction, washed acid-free with water, dried and recrystallized from the appropriate solvent.

R-key and data of **6a-p**: Table 2.

5-Benzyl-4-hydroxy-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazol-6-one (6h). From tetrahydrocarbazole **4a** and *bis*(2,4,6-trichlorophenyl) 2-benzylmalonate (**5i**) (Method C, ''active malonate'' method [15]):

Bis*(2,4,6-trichlorophenyl) 2-benzylmalonate (**5i**).* A mixture of dry 2-benzylmalonic acid (**5**, $R^3 = CH_2Ph$, X = OH) (38.8 g, 0.2 mol), 2,4,6-trichlorophenol (63.2 g, 0.32 mol) and phosphoryl chloride (64.4 g, 0.42 mol) was heated under reflux until the evolution of hydrogen chloride gas had stopped (about 4–6 h). The reaction mixture was then poured onto crushed ice (600 mL), filtered by suction, the solid washed with ice-water, dissolved in toluene (400 mL) and washed with aqueous sodium hydrogencarbonate solution (5%) and water. The organic layer was dried with sodium sulfate and the solvent removed under reduced pressure. The residue was triturated with hexane, filtered and dried at room temperature. The yield was 44.6 g (50%), light yellowish prisms, mp 104°C (lit. mp 106–107°C [15a]).

*5-Benzyl-4-hydroxy-8,9,10,11-tetrahydropyrido[3,2,1:jk]carbazol-6-one (**6h**).* An intimate mixture of tetrahydrocarbazole **4a** (3.75 g, 22 mmol) and *bis*(2,4,6-trichlorophenyl) 2-benzylmalonate (**5i**) (12.1 g, 22 mmol) was heated without solvent for 60 min to 250°C. The 2,4,6-trichlorophenol vapors were removed *via* a funnel into the water pump. After cooling the dark reaction mixture was washed with hexane until the product became semi-solid. Then the product was stirred overnight with aqueous sodium hydroxide solution (0.5*M*, 500 mL), filtered, the filtrate extracted with toluene (2 × 100 mL) and the aqueous phase acidified with concentrated hydrochloric acid. The precipitate was washed with water, recrystallized from glacial acetic acid/water and dried. The yield was 2.17 g (30%).

From tetrahydrocarbazole 4a and 2-benzyl-2-(chlorocarbonyl)ethylketene (5j) (Method D, ''(chlorocarbonyl)ethylketene''-method [16]). *2-Benzyl-2-(chlorocarbonyl)ethylketene (5j).* To a solution of 2-benzylmalonic acid (**5**, $R^3 = CH_2Ph$, X = OH) (38.8 g, 0.2 mol) in toluene (50 mL), thionyl chloride (59.5 g, 0.6 mol) was added dropwise under stirring in a nitrogen atmosphere. The mixture was heated for 24 h under reflux, then toluene and excess thionyl chloride were removed by distillation under reduced pressure (60°C, 130 mm Hg). The residue was distilled under reduced pressure (134–140°C, 15 mm Hg). The yield was 27.2 g (70%) yellowish oil; lit. bp 110–112°C (1.5 mm Hg) [16b].

5-Benzyl-4-hydroxy-8,9,10,11-tetrahydropyrido[3,2,1:jk]carbazol-6-one (6h). To a solution of tetrahydrocarbazole **4a** (5.12 g, 30 mmol) in dry ethyl acetate (150 mL), 2-benzyl-2-(chlorocarbonyl)ketene (**5j**) (6.5 g, 33 mmol) and dry triethylamine (4.5 mL) was added at 40–50°C. The yellow reaction mixture turned red and viscous and a small amount of a dark solid precipitated. The reaction mixture was kept for 30 min at room temperature, then the precipitate was filtered off, the filtrate taken to dryness under reduced pressure and triturated with xylene. The resulting precipitate was filtered by suction and dried. The yield was 5.42 g (55%), yellowish prisms. Data of **6h**: Table 2.

5-Nitro-5-phenyl-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazole-4,6-dione (9). A solution of 4-hydroxy-pyridocarbazole **6a** (2.00 g, 6.3 mmol) in glacial acetic acid (12 mL) was treated with concentrated nitric acid (1.2 mL) and sodium nitrite (0.03 g). The mixture was stirred for 30 min at room temperature, then diluted with ice/water (45 mL), the formed yellow precipitate separated by suction filtration and washed with water until acid-free. The yield was 1.70 g (75%), yellow prisms, mp 164°C (methanol). IR: 2960–2860 w, 1730 s (4-C=O), 1695 s (6-C=O), 1660 sh, 1625 w, 1590 w, 1570 s cm^{-1}; ^1H NMR (CF_3COOH): δ 1.80–2.10 (m, 4 H, 9-CH_2, 10-CH_2), 2.70 (t, $J = 7.0$ Hz, 2 H, 11-CH_2), 3.15 (t, $J = 7.0$ Hz, 2 H, 8-CH_2), 7.25 (t, $J = 7.1$ Hz, 1 H, 2-H), 7.35–7.50 (m, 3 H, PhH), 7.55–7.60 (m, 2 H, PhH), 7.70 (d, $J = 7.1$ Hz, 1-H), 7.90 (d, $J = 7.1$ Hz, 1 H, 8-H). Anal. calcd. for $C_{21}H_{16}N_2O_4$ (360.37): C, 69.99; H, 4.48; N, 7.77. Found: C, 70.34; H, 4.71; N, 7.45.

5-Hydroxy-5-methyl-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazol-4,6-dione (10). A solution of 4-hydroxy-pyridocarbazole **6a** (0.68 g, 2.7 mmol) in aqueous sodium hydroxide solution (0.25*M*, 60 mL) was slowly brought to pH ~8 with aqueous potassium dihydrogenphosphate solution (1*M*, ~10 mL), then hydrogenperoxide (30%, 20 mL) was added. The reaction mixture was stirred for 6 h at 40°C. After cooling to room temperature, the mixture was poured onto crushed ice/water (100

mL), the solid filtered by suction and washed with water. The yield was 0.52 g (72%), yellow prisms, mp 189°C (ethanol). IR: 3395 s, 2945 m, 1711 s (4-C=O), 1684 s (6-C=O), 1630 w, 1593 m cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.49 (s, 3 H, 5-Me), 1.82–1.88 (m, 4 H, 9-CH_2, 10-CH_2), 2.68 (t, J = 7.0 Hz, 2 H, 11-CH_2), 3.06 (t, J = 7.0 Hz, 2 H, 8-CH_2), 6.15 (s, 1 H, 5-OH), 7.41 (t, J = 7.6 Hz, 1 H, 2-H), 7.69 (d, J = 7.6 Hz, 1 H, 1-H), 7.82 (d, J = 7.6 Hz, 1 H, 3-H); MS [APCI, pos]: m/e (%) = 271 (11), 270 (M, 100). Anal. calcd. for $C_{16}H_{15}NO_3$ (269.30): C, 71.36; H, 5.61; N, 5.20. Found: C, 71.20; H, 5.86; N, 5.22.

5-Chloro-5-methyl-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazol-4,6-dione (11a). To a suspension of 4-hydroxy-pyridocarbazole **6a** (2.30 g, 9 mmol) in dioxane (50 mL) at 20°C, sulfuryl chloride (0.8 mL, 10 mmol) was added slowly. The reaction mixture was stirred for 5 h at room temperature and then poured onto crushed ice/water (200 mL). The solid was filtered and washed with water. The yield was 2.00 g (76%), yellow needles, mp 182°C (ethanol). IR: 3432 s, 2936 m, 1722 s (4-C=O), 1689 s (6-C=O), 1629 w, 1592 w cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.74–1.82 and 1.86–1.94 (2 m, 4 H, 9-CH_2 and 10-CH_2), 1.98 (s, 3 H, 5-Me), 2.70 (t, J = 7.0 Hz, 2 H, 11-CH_2), 3.06 (t, J = 7.0 Hz, 2 H, 8-CH_2), 7.45 (t, J = 7.6 Hz, 1 H, 2-H), 7.78 (d, J = 7.6 Hz, 1 H, 1-H), 7.81 (d, J = 7.6 Hz, 1 H, 3-H). Anal. calcd. for $C_{16}H_{14}ClNO_2$ (287.75): C, 66.79; H, 4.90; N, 4.87. Found: C, 66.90; H, 4.92; N, 4.85.

5-Chloro-5-phenyl-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazole-4,6-dione (11b). To a suspension of 4-hydroxy-pyridocarbazole **6g** (1.65 g, 5.2 mmol) in dioxane (25 mL) at 50°C, sulfuryl chloride (1.70 g ~1.01 mL, 12.6 mmol) was added slowly. The mixture was stirred for 10 min, heated to boiling for a few min and then poured onto crushed ice/water (50 mL). The oily product was stirred and washed several times with water until solid. The yellow-orange precipitate was crushed, filtered by suction and washed with water. The yield was 1.79 g (97%), yellow prisms, mp 116°C (ethanol). IR: 3430 s, 2935 m, 1720 s (4-C=O), 1690 s (6-C=O), 1630 w cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.75–1.83 and 1.85–1.93 (2 m, 4 H, 9-CH_2 and 10-CH_2), 2.71 (t, J = 7.0 Hz, 2 H, 11-CH_2), 3.05–3.09 (m, 2 H, 8-CH_2), 7.37–7.50 (m, 4 H, 3 PhH, 2-H), 7.55–7.60 (m, 2 H, PhH), 7.75–7.85 (m, 2 H, 1-H, 3-H). Anal. calcd. for $C_{21}H_{16}ClNO_2$ (349.82): C, 72.10; H, 4.61; N, 4.00. Found: C, 72.36; H, 4.32; N, 4.25.

5-Chloro-2,5,9-trimethyl-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazole-4,6-dione (11c). From 4-hydroxy-pyridocarbazole **6l** (5.06 g, 18 mmol) in dioxane (100 mL) and sulfuryl chloride (2.7 g ~1.61 mL, 20 mmol) as described for **11a**. Work-up was performed as described for **11b**. The yield was 4.56 g (80%) orange-yellow needles, mp 151°C (ethanol). IR: 3435 s, 2949 m, 2923 m, 1719 s (4-C=O), 1690 s (6-C=O), 1630 w, 1604 w cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.12 (d, J = 7.0 Hz, 3 H, 9-Me), 1.46–1.50 (m, 1 H, 9-H), 1.96–1.98 (m, 5 H, 5-Me, 10-CH_2), 2.51 (s, 3 H, 2-Me), 2.59–2.70 and 2.72–2.83 (2 m, 4 H, 11-CH_2, 8-CH_2), 7.58 (s, 1 H, 1-H), 7.67 (s, 1 H, 3-H). Anal. calcd. for $C_{18}H_{18}ClNO_2$ (315.80): C, 68.46; H, 5.75; N 4.44. Found: C, 68.58; H, 5.59; N 4.39.

2,5-Dichloro-5-phenyl-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazole-4,6-dione (11d). From 4-hydroxy-pyridocarbazole **6n** (1.50 g, 4.3 mmol) in dioxane (25 mL) and sulfuryl chloride (0.70 g–0.42 mL, 5.2 mmol) as described for **11b**. The yield was 1.42 g (86%) yellow prisms, mp 100°C (ethanol). IR: 3430 s, 2950 m, 2920 m, 1720 s (4-C=O), 1690 s (6-C=O), 1630 w, 1605 w cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.75–1.82 and 1.85–1.92 (2 m, 4 H, 9-CH_2 and 10-CH_2), 2.70 (t, J = 7.0 Hz, 2 H, 11-CH_2), 3.05–3.08 (m, 2 H, 8-CH_2), 7.35–7.50 (m, 3 H, 3 PhH), 7.55–7.60 (m, 2 H, PhH), 7.80–8.00 (m, 2 H, 1-H, 3-H). Anal. calcd. for $C_{21}H_{15}Cl_2NO_2$ (384.27): C, 65.64; H, 3.93; N. 3.65. Found: C, 65.28; H, 3.95; N 3.27.

2,5-Dichloro-10-methyl-5-phenyl-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazole- 4,6-dione (11e). From 4-hydroxy-pyridocarbazole **6o** (1.10 g, 3 mmol) in dioxane (20 mL) and sulfuryl chloride (0.49 g, 0.30 mL, 3.7 mmol) as described for **11b**. The yield was 1.10 g (91%), yellow prisms, mp 105°C (ethanol). IR: 3420 s, 2940 m, 2910 m, 1715 s (4-C=O), 1690 s (6-C=O), 1625 w, 1605 w cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.06 (d, J = 7.0 Hz, 3 H, 10-Me), 1.30–1.55 (m, 1 H, 10-H), 1.75–2.00 (m, 2 H, 9-CH_2), 2.70 (t, J = 7.0 Hz, 2 H, 11-CH_2), 3.03–3.08 (m, 2 H, 8-CH_2), 7.35–7.50 (m, 3 H, 3 PhH), 7.55–7.60 (m, 2 H, PhH), 7.81 (d, J = 2.0 Hz, 1 H, 1-H), 8.02 (d, J = 7.0 Hz, 1 H, 3-H). Anal. calcd. for $C_{22}H_{17}Cl_2NO_2$ (398.29): C, 66.34; H, 4.30; N, 3.52; Found: C, 66.25; H, 4.28; N, 3.24.

5-Azido-5-methyl-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazole-4,6-dione (12). A suspension of 5-chloropyridocarbazole **11a** (1.20 g, 4.2 mmol) and sodium azide (1.00 g, 15.3 mmol) in dimethylformamide (40 mL) was stirred and heated for 1 h at 50°C. After cooling to room temperature, the mixture was poured onto crushed ice/water (100 mL), filtered by suction and washed with water. The yield was 0.95 g (77 %) yellow needles, mp 131°C (ethanol). IR: 3432 s, 2929 m, 2144 sh, 2106 s (N_3), 1722 s (4-C=O), 1688 s (6-C=O), 1626 w, 1592 m cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.70 (s, 3 H, 5-Me), 1.81–1.83 and 1.85–1.88 (2 m, 4 H, 9-CH_2, 10-CH_2), 2.69 (t, J = 7.0 Hz, 2 H, 11-CH_2), 3.05–3.09 (m, 2 H, 8-CH_2), 7.43 (t, J = 7.6 Hz, 1 H, 2-H), 7.72 (d, J = 7.5 Hz, 1 H, 1-H), 7.85 (d, J = 7.5 Hz, 1 H, 3-H). Anal. calcd. for $C_{16}H_{14}N_4O_2$ (294.32): C, 65.30; H, 4.79; N, 19.04. Found: C, 65.24; H, 4.78; N, 18.65.

5-Benzylamino-5-methyl-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazole-4,6-dione (14a). A solution of 5-chloropyridocarbazole **11a** (1.20 g, 4.2 mmol) and benzylamine (**13a**) (0.50 mL, 4.5 mmol) in dimethylformamide (3 mL) was heated and stirred for 15 h at 50°C. After cooling to room temperature, the mixture was poured onto ice/water (100 mL), filtered by suction and washed with water. The yield was 1.22 g (81%), yellow prisms, mp 73°C (ethanol). IR: 3395 m, 2932 m, 2853 w, 1720 s (4-C=O), 1681 s (6-C=O), 1628 w, 1591 m cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.50 (s, 3 H, 5-Me), 1.79–1.83 and 1.86–2.08 (2 m, 4 H, 9-CH_2, 10-CH_2), 2.67 (t, J = 7.0 Hz, 2 H, 11-CH_2), 3.04–3.14 (m, 2 H, 8-CH_2), 3.51 (s, 2 H, benzyl-CH_2), 7.17–7.30 (m, 5 H, PhH), 7.43 (t, J = 7.7 Hz, 1 H, 2-H), 7.70 (d, J = 7.5 Hz, 1 H, 1-H), 7.81 (d, J = 7.6 Hz, 1 H, 3-H); MS [APCI, pos]: m/e (%) = 360 (11), 359 (100, M). Anal. calcd. for $C_{23}H_{22}N_2O_2$ (358.44): C, 77.07; H, 6.19; N, 7.82. Found: C, 77.35; H, 5.99; N, 7.54.

5-Methyl-5-phenylamino-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazole-4,6-dione (14b). From a solution of 5-chloropyridocarbazole **11a** (1.00 g, 3.4 mmol) and aniline (**13b**) (0.5 mL, 5.5 mmol) in dimethylformamide (20 mL) as described for **14a**. The yield was 0.63 g (54 %), yellow prisms, mp 115°C (ethanol). IR: 3395 m, 2932 m, 2856 w, 1724 s (4-C=O), 1686 s (6-C=O), 1603 m, 1592 m cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.65 (s, 3 H, 5-Me), 1.83–1.91 (m, 4 H, 9-CH_2, 10-

CH_2), 2.73 (t, J = 7.0 Hz, 2 H, 11-CH_2), 3.06 (t, J = 7.0 Hz, 2 H, 8-CH_2), 6.12 (d, J = 8.0 Hz, 2 H, PhH), 6.51 (t, J = 7.3 Hz, 1 H, PhH), 6.86 (s, 1 H, NH, D_2O-exchangeable), 6.94 (t, J = 7.8 Hz, 2 H, PhH), 7.51 (t, J = 7.6 Hz, 1 H, 2-H), 7.76 (d, J = 7.6 Hz, 1 H, 1-H), 7.93 (d, J = 7.6 Hz, 1 H, 3-H). Anal. calcd. for $C_{22}H_{20}N_2O_2$ (344.42): C, 76.72; H, 5.85; N, 8.13. Found: C, 76.39; H, 5.67; N, 8.36.

5-Methyl-5-morpholino-8,9,10,11-tetrahydropyrido[3,2,1-jk] carbazole-4,6-dione (16a). A solution of 5-chloropyridocarbazole **11a** (1.60 g, 5.5 mmol) and morpholine (**15a**) (0.5 mL, 5.7 mmol) in dimethylformamide (20 mL) was stirred for 5 h at 50°C. After cooling to room temperature, the mixture was poured into water (100 mL), the solid was filtered by suction, washed with water and dried at room temperature in vacuo. The yield was 1.40 g (75%), yellow prisms, mp 72°C (ethanol). IR: 3425 m, 2936 s, 2853 s, 1713 s (4-C=O), 1681 s (6-C=O), 1631 w, 1591 m cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.49 (s, 3 H, 5-Me), 1.78–1.81 and 1.86–1.89 (2 m, 4 H, 9-CH_2, 10-CH_2), 2.55–2.60 (m, 4 H, 2x 5-morpholino-CH_2), 2.67 (t, J = 7.0 Hz, 2 H, 11-CH_2), 3.09 (s, J = 7.0 Hz, 2 H, 8-CH_2), 3.49 (t, J = 4.2 Hz, 4 H, 2x 5-morpholino-CH_2), 7.40 (t, J = 7.6 Hz, 1 H, 2-H), 7.66 (d, J = 7.6 Hz, 1 H, 1-H), 7.82 (d, J = 7.6 Hz, 1 H, 3-H); MS [APCI, pos]: m/e (%) = 340 (28), 339 (100, M), 337 (12). Anal. calcd. for $C_{20}H_{22}N_2O_3$ (338.41): C, 70.99; H, 6.55; N, 8.28. Found: C, 71.24; H, 6.32; N, 8.01.

5-Methyl-5-piperidino-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazole-4,6-dione (16b). From 5-chloropyridocarbazole **11a** (1.50 g, 5.2 mmol) and piperidine (**15b**) (0.6 mL, 6 mmol) in dimethylformamide (20 mL) as described for **16a**. The yield was 1.45 g (84%), yellow prisms, mp 87°C (ethanol). IR: 3421 m, 2934 s, 2851 m, 1714 s (4-C=O), 1681 s (6-C=O), 1630 w, 1591 m cm^{-1}: ^1H NMR (DMSO-d_6): δ = 1.31–1.33 and 1.38–1.40 (2 m, 6 H, 3 5-piperidino-CH_2), 1.47 (s, 3 H, 5-Me), 1.77–1.80 and 1.85–1.87 (2 m, 4 H, 9-CH_2, 10-CH_2), 2.54–2.57 (m, 4 H, 5-piperidine-CH_2), 2.67 (t, J = 7.0 Hz, 2 H, 11-CH_2), 3.09 (t, J = 7.0 Hz, 2 H, 8-CH_2), 7.39 (t, J = 7.6 Hz, 1 H, 2-H), 7.65 (d, J = 7.5 Hz, 1 H, 1-H), 7.80 (d, J = 7.6 Hz, 1 H, 3-H); MS [APCI, pos]: m/e (%) = 338 (20%), 337 (M, 100%). Anal. calcd. for $C_{21}H_{24}N_2O_2$ (336.44): C, 74.97; H, 7.19; N, 8.33. Found: C, 75.35; H, 7.01; N, 8.04.

4-Benzylamino-5-methyl-8,9,10,11-tetrahydropyrido[3,2,1-jk] carbazol-6-one (17a). A solution of 4-hydroxy-pyridocarbazole **6a** (2.53 g, 10 mmol) and excess benzylamine (**13a**) (20 mL) was heated for 6 h at 180°C using an air condenser to remove water formed during the reaction, cooled and the excess benzylamine removed by distillation in vacuo. To the liquid residue petroleum ether (bp 60–90°C, 50 mL) was added and stirred. The solid precipitated, was filtered by suction and washed with petroleum ether (bp 60–90°C). Then toluene (50 mL) was added and the solid was filtered by suction and washed with ethanol (20 mL). The yield was 2.15 g (63 %), yellow prisms, mp 128°C (ethanol). IR: 3442 m, 3386 s, 3357 s, 2934 m, 1642 m (6-C=O), 1618 s, 1536 s cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.89–1.90 and 1.96–1.97 (2 m, 4 H, 9-CH_2, 10-CH_2), 2.18 (s, 3 H, 5-Me), 2.76 (t, J = 6.0 Hz, 2 H, 11-CH_2), 3.27 (t, J = 6.0 Hz, 2 H, 8-CH_2), 4.43 (s, 1 H, NH), 4.82 (d, J = 3.8 Hz, 2 H, benzyl-CH_2), 7.30–7.36 (m, 3 H, PhH, 2-H), 7.38–7.40 (m, 3 H, PhH), 7.61 (d, J = 7.5 Hz, 1 H, 1-H), 7.67 (d, J = 8.0 Hz, 1 H, 3-H). ^{13}C NMR ($CDCl_3$): δ 11.2, 21.2 and 22.4 (C9, C10), 23.0 and 24.9 (C11, C8), 52.5 (Me), 108.5, 113.7, 117.4, 118.5, 120.4, 122.4, 127.5, 128.1, 129.9, 131.2 (13 ArC), 137.7, 139.1, 150.2 (3 C—N), 161.6 (C=O); MS [APCI, pos]: m/e (%) = 344 (25), 343 (100), 341(5), 241 (33), 108 (39). Anal. calcd. for $C_{23}H_{22}N_2O$ (342.44): C, 80.67; H, 6.48; N, 8.18. Found: C, 80.38; H, 6.47; N, 8.27.

5-Methyl-4-phenylamino-8,9,10,11-tetrahydropyrido[3,2,1-jk] carbazole-6-one (17b). From 4-hydroxy-pyridocarbazole **6a** (2.53 g, 10 mmol), aniline hydrochloride (2.50 g, 19 mmol) and aniline (**13b**) (20 mL) as described for **17a**. The yield was 2.10 g (64 %), yellowish prisms, mp 167°C (ethanol). IR: 3462 m, 3342 m, 2934 m, 1648 m (6-C=O), 1630 s, 1601 m, 1555 w cm^{-1}; ^1H NMR($CDCl_3$): δ 1.89–1.93 and 1.96–2.00 (2 m, 4 H, 9-CH_2. 10-CH_2), 2.15 (s, 3 H, 5-Me), 2.78 (t, J = 6.0 Hz, 2 H, 11-CH_2), 3.31 (t, J = 6.0 Hz, 2 H, 8-CH_2), 6.02 (s, 1 H, NH), 6.94 (d, J = 7.6 Hz, 2 H, PhH), 7.01 (t, J = 7.4 Hz, 1 H, 2-H), 7.15–7.29 (m, 3 H, PhH), 7.38 (d, J = 7.8 Hz, 1 H, 1-H), 7.58 (d, J = 7.5 Hz, 1 H, 3-H); ^{13}C NMR ($CDCl_3$): δ 12.4, 21.3, 22.4, (C9, C10), 22.9, 24.8 (C8, C11), 42.0 (Me), 114.9, 117.8, 118.4, 118.7, 119.2, 120.5, 127.9, 129.2, 131.3 (12 ArC), 137.6, 143.5, 144.3 (3 C—N), 161.8 (C=O); MS [APCI, pos]: m/e (%) = 330 (28), 329 (100). Anal. calcd. for $C_{22}H_{20}N_2O$ (328.42): C, 80.46; H, 6.14; N, 8.53. Found: C, 80.20; H, 6.26; N, 8.68.

4-Chloro-5-methyl-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazole-6-one (18a). A solution of 4-hydroxy-pyridocarbazole **6a** (2.53g, 10 mmol) in phosphoryl chloride (30 mL) was heated under reflux for 1 h. The excess phosphoryl chloride was removed i. vac., the residue cooled to room temperature and poured onto crushed ice/water (100 mL). Caution: strong exothermic reaction. The product was brought to pH ~4 to 6 with 2*M* aqueous sodium hydroxide solution, the solid filtered by suction and washed with water. The yield was 1.40 g (51 %), ash–grey powder, mp 165°C (ethanol). IR: 3453 m, 2930 s, 1659 s (6-C=O), 1628 m, 1597 w cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.87–2.01 (m, 4 H, 9-CH_2, 10-CH_2), 2.41 (s, 3 H, 5-Me), 2.76 (t, J = 6.0 Hz, 2 H, 11-CH_2), 3.24 (t, J = 6.0 Hz, 2 H, 8-CH_2), 7.42 (t, J = 7.7 Hz, 1 H, 2-H), 7.63 (d, J = 7.6 Hz, 1 H, 1-H), 7.73 (d, J = 7.8 Hz, 1 H, 3-H); MS [APCI, pos]: *m/z* (%) = 274 (35), 273 (15), 272 (100, M). Anal. calcd. for $C_{16}H_{14}ClNO$ (271.75): C, 70.72; H, 5.19; N, 5.00. Found: C, 70.49; H, 5.26; N, 5.15

4-Chloro-5-phenyl-8,9,10,11-tetrahydro-pyrido[3,2,1-jk]carbazol-6-one (18b). From 4-hydroxy-pyridocarbazole **6g** (3.15 g, 10 mmol) and phosphoryl chloride (30 mL) as described for **18a**. The yield was 2.20 g (66%), light brownish needles, mp 154°C (ethanol). IR: 2960–2840 w, 1660 s (6-C=O), 1625 w, 1595 w cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.85–2.00 (m, 4 H, 9-CH_2, 10-CH_2), 2.75 (t, J = 6.0 Hz, 2 H, 11-CH_2), 3.20–3.25 (m, 2 H, 8-CH_2), 7.35–7.50 (m, 4 H, 3 PhH, 2-H), 7.55–7.60 (m, 2 H, PhH), 7.65–7.75 (m, 2 H, 1-H, 3-H). Anal. calcd. for $C_{21}H_{16}ClNO$ (333.82): C, 75.56; H, 4.83; N, 4.20. Found: C, 75.39; H, 5.06; N, 4.05.

5-Benzyl-4-chloro-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazol-6-one (18c). From 4-hydroxy-pyridocarbazole **6h** (3.29 g, 10 mmol) and phosphoryl chloride (30 mL) as described for **18a**. The yield was 0.79 g (24%), yellow prisms, mp 106°C (ligroin). IR: 2950-2850 w, 1655 s (6-C=O), 1615 w, 1590 w; ^1H NMR (DMSO-d_6): δ 1.70–1.90 (m, 4 H, 2 CH_2), 2.70 (s, 2 H, 11-CH_2), 3.10 (s, 2 H, 8-CH_2), 4.00 (s, benzyl-CH_2), 7.10–7.50 (m, 6 H, 5 benzyl-H, 2-H), 7.70 (d, J = 6.0 Hz, 1-H), 8.05 (d, J = 6.0 Hz, 3-H). Anal. calcd. for $C_{22}H_{18}ClNO$

(347.85): C, 75.97; H, 5.22; N, 4.03. Found: C, 76.32; H, 4.91; N, 3.65.

2,4-Dichloro-10-methyl-5-phenyl-8,9,10,11-tetrahydro-pyrido [3,2,1-jk]carbazol-6-one (18d). From 4-hydroxy-pyridocarbazole **6o** (3.63 g, 10 mmol) and phosphoryl chloride (30 mL) as described for **18a**. The yield was 3.28 g (86%), colorless prisms, mp 190°C (ethanol). IR: 2930–2800 w, 1660 s, 1610 w, 1590 w cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.85–2.05 (m, 4 H, 9-CH_2, 10-CH_2), 2.73 (t, J = 6.0 Hz, 2 H, 11-CH_2), 3.20–3.25 (m, 2 H, 8-CH_2), 7.35–7.45 (m, 3 H, 3 PhH), 7.55–7.60 (m, 2 H, PhH), 7.65–7.75 (m, 2 H, 1-H, 3-H). Anal. calcd. for $C_{22}H_{17}Cl_2NO$ (382.29): C, 69.12; H, 4.48; N, 3.66. Found: C 69.18; H, 4.81; N 3.80.

4-Chloro-2,5,9-trimethyl-8,9,10,11-tetrahydropyrido[3,2,1-jk] carbazol-6-one (18e). From 4-hydroxy-pyridocarbazole **6l** (2.81 g, 10 mmol) and phosphoryl chloride (30 mL) as described for **18a**. The yield was 1.85 g (62%), colorless prisms, mp 157°C (ethanol). IR: 3450 m, 2922 m, 1662 s (6-C=O), 1627 m, 1588 w cm^{-1}. ^1H NMR ($CDCl_3$): 1.15 (d, 3 H, 9-Me), 1.41–1.46 (m, 1 H, 9-H), 1.89–2.19 (m, 2 H, 10-CH_2), 2.41 (s, 3 H, 5-Me) 2.58 (s, 3 H, 2-CH_3), 2.68–2.84 (m, 4 H, 8-CH_2, 11-CH_2), 7.46 (d, J = 6.5 Hz, 1 H, 1-H), 7.55 (d, J = 6.5 Hz, 1 H, 3-H). Anal. calcd. for $C_{18}H_{18}ClNO$ (299.80): C, 72.11; H, 6.05; N, 4.67. Found: C, 71,81; H, 5,94; N, 4,51.

4-Azido-5-methyl-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazole-6-one (19a). *Method A*. A mixture of 4-chloro-pyridocarbazole **18a** (1.36 g, 5 mmol) and sodium azide (0.98 g, 15 mmol) in dimethylformamide (30 mL) was intensively stirred and heated for 36 h at 50°C. After cooling to room temperature, the mixture was poured onto crushed ice/water (250 mL). This solution was kept for 3 h at room temperature, filtered by suction and dried in vacuum with phosphorouspentoxide. Tlc check showed a mixture of starting **18a** and azide **19a**, which were separated by dry column flash chromatography (hexane/ethyl acetate as gradients). The yield of **19a** was 0.33 g (15%). *Method B*. A mixture of 4-hydroxy-pyridocarbazole **6a** (0.50 g, 2 mmol) and sodium azide (0.65 g, 10 mmol) in excess phosphoryl chloride (3 mL ~5 g, 30 mmol) was intensively stirred and heated for 12 h at 60°C. The excess phosphoryl chloride was removed by vacuum distillation. After cooling to room temperature, the solid was poured into crushed ice/water (50 mL), and filtered by suction. The yield was 0.32 g (58 %), yellowish crystals, mp 104°C (dec.) (methanol). IR: 3432 m, 2390 m, 2855 w, 2114 s (N_3), 1661 s (6-C=O), 1626 m, 1598 w cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.88–1.82 and 1.87–1,89 (2 m, 4 H, 9-CH_2, 10-CH_2), 2.32 (s, 3 H, 5-Me), 2.72 (t, J = 7.0 Hz, 2 H, 11-CH_2), 3.10 (t, J = 7.0 Hz, 2 H, 8-CH_2), 7.48 (t, J = 7.7 Hz, 1 H, 2-H), 7.72 (d, J = 7.6 Hz, 1 H, 1-H), 7.78 (d, J = 7.8 Hz, 1 H, 3-H). Anal. calcd. for $C_{16}H_{14}N_4O$ (278.32): C, 69.05; H, 5.07; N, 20.13. C, 69.41; H, 5.44; N, 19.75.

4-Azido-5-phenyl-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazol-6-one (19b). To a solution of 4-chloro-pyridocarbazole **18b** (0.60 g, 1.8 mmol) in dimethylformamide (30 mL) at 50°C, sodium azide (0.5 g, 7.2 mmol) was added and the mixture stirred for 12 h at room temperature, and then for about 60 min at 80°C until the reaction was finished (tlc check). The yield was 0.20 g (33%), brownish prisms, mp 107°C (dec.). IR: 3430 m, 2350 m, 2850 w, 2115 s (N_3), 1660 s (6-C=O), 1625 m, 1595 w cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.85–2.05 (m, 4 H, 9-CH_2, 10-CH_2), 2.70 (t, J = 6.0 Hz, 2 H, 11-CH_2), 3.20–3.25 (m, 2 H, 8-CH_2), 7.35–7.50 (m, 4 H, 3 PhH, 2-H), 7.55–7.62 (m, 2 H, PhH), 7.67–7.80 (m, 2 H, 1-H, 3-H). Anal. calcd. for $C_{21}H_{16}N_4O$ (340.39): C, 74.10; H, 4.74; N, 16.46. Found: C, 74.35; H, 4.52; N, 16.28.

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