Synthesis and Characterization of the Biologically Active 2-[1-(4-Chlorobenzyl)-1*H*-indol-3-yl]-2-oxo-*N*-pyridin-4-yl Acetamide

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Dedicated to Professor Dr. A. Kleemann on the occasion of his 60th birthday

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The spectroscopic characterization of the new potent tubulin inhibitor 2-[1-(4-chlorobenzyl)-1*H*-indol-3-yl]-2-oxo-*N*-pyridin-4-yl acetamide (D-24851) (**7**), which is under preclinical development, is described. The synthesis was optimized and follows a straightforward route from the unsubstituted indole via the 1-(4-chlorobenzyl)-indole (**3**) and the indol-3-yl-2-oxo-acetyl chloride (**5**) to the indol-3-yl-2-oxo acetamide product. The structure was assigned by sophisticated NMR experiments, for example a 1,1-ADEQUATE experiment, and X-ray crystallography.

Introduction

Despite much progress in the diagnosis and treatment of malignant diseases, we are still faced with some significant deficits in finding an effective and tolerable drug treatment, especially in the treatment of serious solid tumors. Thus the search for new anti-tumor active agents is of great importance.

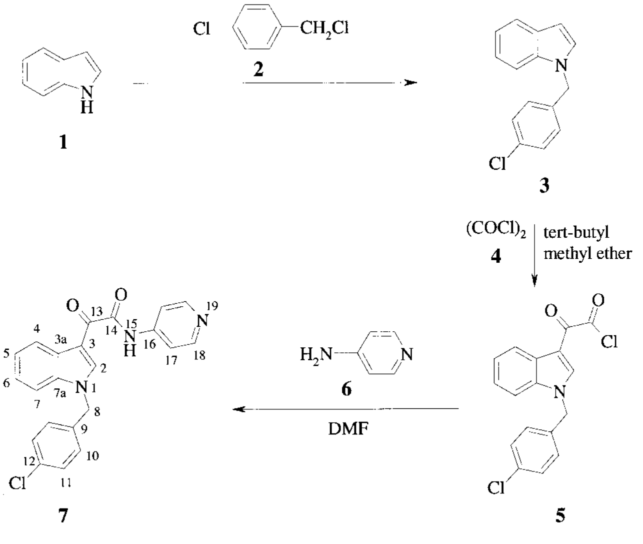
It is possible to target and destroy dividing cancer cells by intervening during the stages of mitosis, where microtubules play an important role in the M-phase of the cell replication. Obviously the microtubule system is an attractive target for the development of anticancer compounds. Microtubules are protein fibers composed of alternating α- and β-tubulins. Antimitotic agents act by interfering with the dynamic system of tubulin polymerization or depolymerization. These compounds inhibit the cell proliferation by arresting dividing cells in the metaphase. With the specific substituted indol-3-yl-2-oxo acetamides, we have found a new substance class that possesses tubulin-inhibiting properties.[1] The best representative of this substance class until now has been D-24851, a compound with excellent in vitro and in vivo anti-tumor properties.[2] This new, small-molecule tubulin binder is currently in advanced preclinical development and we expect to start phase I clinical trials in the next few months.

In this paper we describe the three step synthesis and the structural elucidation of compound D-24851 by NMR spectroscopy and X-ray analysis.

Results and Discussion

Synthesis

The synthetic scheme employed for the preparation of the target compound 2-[1-(4-chlorobenzyl)-1*H*-indol-3-yl]-2-oxo-*N*-pyridin-4-yl acetamide (D-24851; **7**) is shown in Scheme 1.[3] The reaction of indole **1** with 4-chlorobenzyl chloride **2** in dimethylformamide yielded 1-(4-chlorobenzyl)-1*H*-indole (**3**) in 97% yield. Treatment of **3** with oxalyl chloride **4** in *tert*-butyl methyl ether or diethyl ether as sol-



Scheme 1. Three-step synthesis of 2-[1-(4-chlorobenzyl)-1*H*-indol-3-yl]-2-oxo-*N*-pyridin-4-yl acetamide **7** (D-24851)

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vent gave 2-[1-(4-chlorobenzyl)-1*H*-indol-3-yl]-2-oxoacetyl chloride (**5**) in 90% yield. The aminolysis of **5** with excess 4-aminopyridine (**6**) in dimethylformamide at low temperature afforded the desired 2-[1-(4-chlorobenzyl)-1*H*-indol-3-yl]-2-oxo-*N*-pyridin-4-yl acetamide (**7**) in 64% yield.

Structural Investigation

The structures of the reaction products up to the glyoxylic acid amide **7** (D-24851) have been identified by NMR spectroscopy. The ^{1}H NMR spectrum of 1-(4-chlorobenzyl)-1*H*-indole **3** in [D$_6$]DMSO shows all the expected resonances for the indole and the 4-chlorobenzyl moieties. The absence of the low field NH signal compared to the unsubstituted indole proves the *N*-substitution. After the reaction of **3** with oxalyl chloride **4** to give 2-[1-(4-chlorobenzyl)-1*H*-indol-3-yl]-2-oxoacetyl chloride (**5**), the corresponding ^{1}H NMR spectrum shows the expected multiplets for 4-H, 5-H, 6-H, 7-H, 10-H and 11-H and a singlet for 2-H, supporting the substitution at position 3. Nevertheless a full NMR structural elucidation of **7** in [D$_6$]DMSO was done after the reaction of **5** with 4-aminopyridine (**6**) to prove the structure of the target molecule and especially to exclude the possible exchange of the indole substituents.

All ^{1}H NMR chemical shifts were in accordance with the given structure. The corresponding ^{13}C NMR spectrum showed a resonance for C-8 at $\delta = 49.09$, which agrees well with the N-substitution and not with a solely aromatic-substituted methylene group. The resonances at $\delta = 162.93$ and 180.61 for C-14 and C-13, respectively, also support this structure, as exchanged substituents would yield an oxaldiamide with ^{13}C resonances between approximately $\delta = 165$ 2and 175. Dipolar correlations from 8-H to 10-H and 7-H in the gs-H,H-NOESY[4] spectrum revealed a proximity of these groups and further support the structure. In addition to these results the long range correlations in the gs-HMBC (Heteronuclear Multiple Bond Coherence)[5] and COLOC experiments (COrrelation spectroscopy via LOng range Couplings)[6] between 8-H and C-9, C-10, C-2 and possibly to C-7a (unsure due to signal overlap) again support the N-benzyl structure. An independent proof was gained by the results of a 1,1-ADEQUATE (Adequate sensitivity DoublE QUAnTum spEctroscopy).[7] This gradient-selected experiment shows correlations between the protons bound to car-

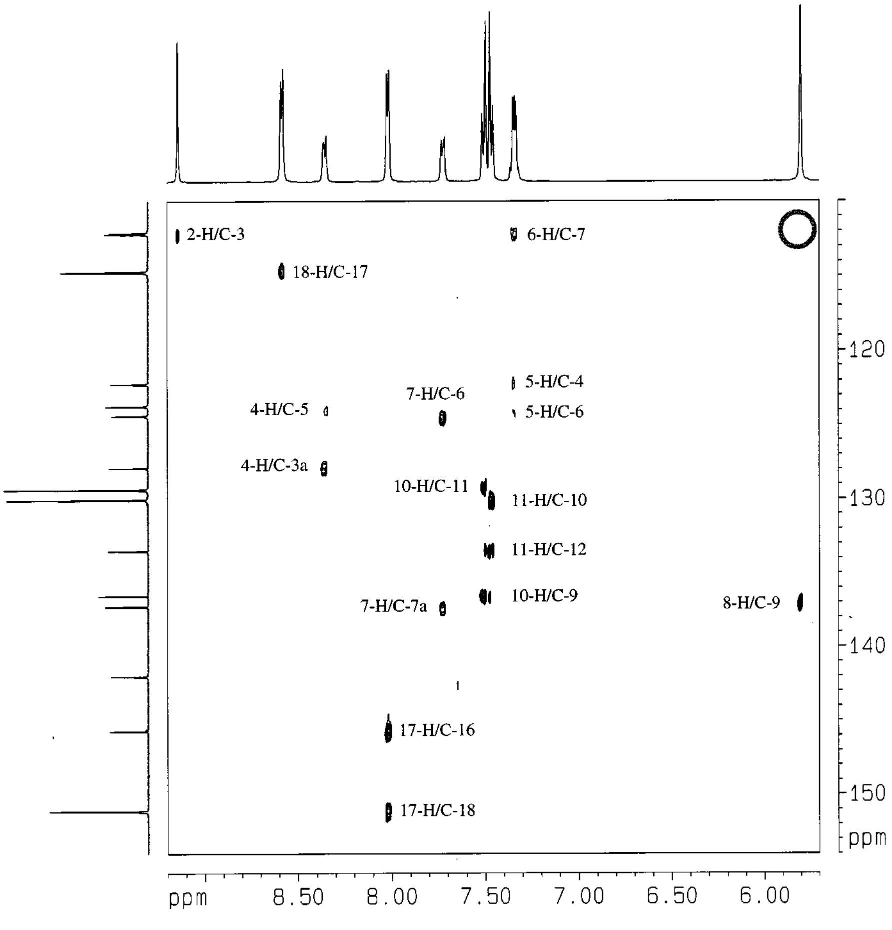

Figure 1. The 1,1-ADEQUATE spectrum of 2-[1-(4-chlorobenzyl)-1*H*-indol-3-yl)-2-oxo-*N*-pyridin-4-yl acetamide (**7**), recorded over 2 days 13 hours with 256 t_1 increments, 352 scans per increment and 2k number of data points in ω_1; relaxation delay 2 s; data were apodized using a $\cos^2$ function in F_2 and a $\pi/3$-shifted $\cos^2$ function in F_1; the delays were optimized to a $^{1}J_{\mathrm{H,C}}$ coupling constant of 140 Hz and a $^{1}J_{\mathrm{C,C}}$ coupling constant of 55 Hz; assignments are annotated according to the numbering of Scheme 1, the missing correlation which would have proved a different substitution is marked by the circle

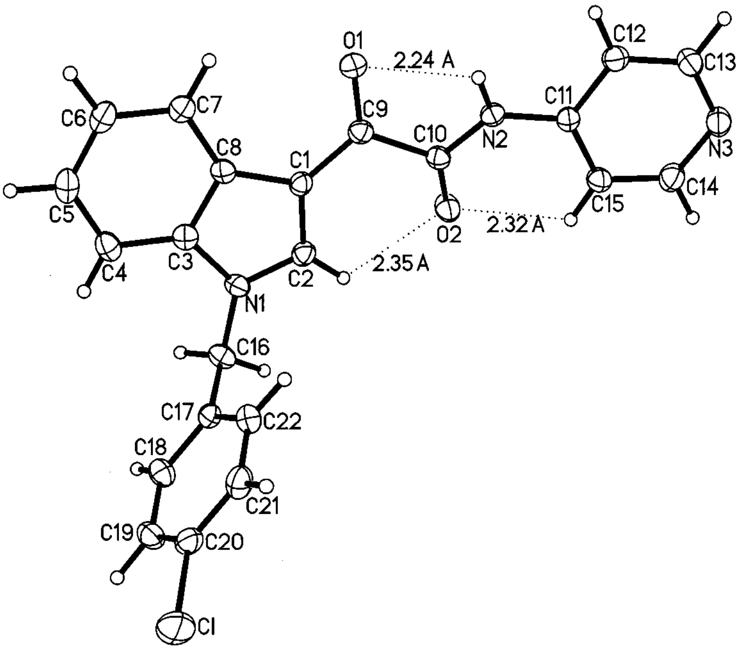

Figure 2. Perspective view of molecule **7**, shown with 50% probability ellipsoids

bon and its geminal carbons and therefore reveals C−C connectivity information. Moreover, it allows us to distinguish between correlations due to the ^2J(H,C) and ^3J(H,C) couplings observed in the HMBC and COLOC experiments. In comparison to its directly detected analogue INADEQUATE (Incredible Natural Abundance DoublE QUAntum Transfer Experiment),[8] a maximum sensitivity gain of a factor of up to 32 can be achieved with the ADEQUATE technique. Due to the low solubility of **7** in DMSO the experiment was performed with a solution in [D_9]*N*-methylpyrrolidinone (NMP). The results of the introductory homo- and heteronuclear one- and two-dimensional NMR experiments in NMP support the results in [D_6]DMSO. In the 1,1-ADEQUATE spectrum (Figure 1) a correlation between 8-H and C-9, but no correlation from 8-H to C-3, was detected, which proves the proposed structure.

In addition to the NMR studies an X-ray analysis was performed. Figure 2 shows a perspective view of molecule **7** as observed in the crystal structure. The indole group is perfectly planar. The angle between the plane of the indole group and the plane of the keto group attached to C(1) is 4° (numbering scheme as in Figure 2). The two keto groups are *trans* positioned with a torsional angle O(1)−C(9)−C(10)−O(2) of −157.6(2)°. The angle between the plane of the trans-amide group and the plane of the pyridine group is 14°. The molecule shows a weak, intramolecular hydrogen bond between the N(2)−H(02) bond and keto oxygen O(1) with dimensions N(2)−H(02): 0.83(2) Å, H(02)···O(1): 2.24(2) Å, N(2)···O(1): 2.654(2) Å and angle N(2)−H(02)−O(1): 111(1)°. Two additional intramolecular O···H distances approach the van der Waals contact distance of 2.4 Å: O(2)···H(2): 2.35(2) Å and O(2)···H(15): 2.32(1) Å. These contacts may be classified as weak, electrostatic interactions. The intramolecular interactions force the molecule, with the exception of the *N*-benzyl group, to be approximately planar. Almost planar conformations, stabilized by similar intramolecular interactions as for the title compound, have been observed in the crystal structures of two glyoxylic acid anilide derivatives.[9] Approximately planar conformations are generally observed in crystal structures containing glyoxylic acid amide groups.[10] The crystal packing of **7** (Figure 3) shows centrosymmetric dimers of molecules connected by intermolecular C(22)−H(22)···N(3) contacts (symmetry code: 1 − *x*, 1 − *y*, 1 − *z*). The intermolecular H(22)···N(3) distances are 2.54(2) Å and are not much longer than the van der Waals

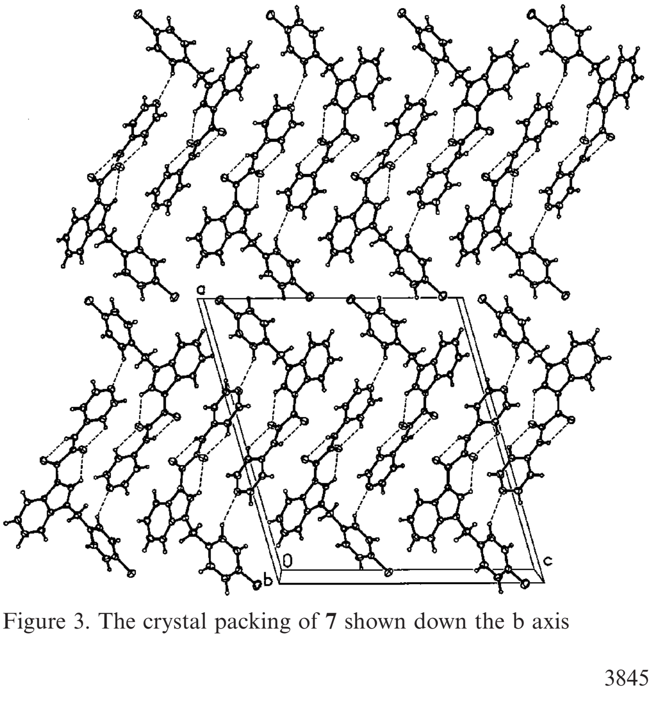

Figure 3. The crystal packing of **7** shown down the b axis

contact distance of 2.5 Å between N and H. These intermolecular contacts may be classified as weak C−H···N hydrogen bonds.[11] There are no other short intra- or intermolecular contacts.

Experimental Section

The NMR spectra were recorded with a Bruker DRX 500 at 500.13 MHz (^{1}H NMR) or 125.77 MHz (^{13}C NMR) at 303 K. Chemical shifts are reported on the δ scale with reference to tetramethylsilane (TMS) as an internal standard (δ = 0). [D$_6$]DMSO with a deuteration grade of greater than 99.8% was purchased from E. Merck, [D$_9$]*N*-methylpyrrolidinone with a deuteration grade of greater than 99% was purchased from euroiso-top. IR spectra were measured with a BioRad FT-IR FTS 135 Infrared spectrometer. The electrospray ionisation mass spectra (ESI-MS) were recorded on a Thermo Quest (Finnigan) LC-Q instrument coupled to a HPLC system HP 1100 (Hewlett Packard) using a reversed-phase chromatography with a linear gradient of acetonitrile/water/trifluoroacetic acid eluent. The electron-impact mass spectra (EI-MS) were run on a Finnigan MAT 95 magnetic sector instrument upon direct evaporation of the samples. Elemental analysis were performed with a Mettler FP1 elemental analyser. The progress of the reactions was monitored by pre-coated TLC Plates silica gel 60 F-254 (Merck, Darmstadt). Merck silica gel (Kieselgel 60) was used for the flash chromatography (230−400 mesh) columns. The X-ray analysis was performed as described below.

1-(4-Chlorobenzyl)-1*H*-indole (3): Indole **1** (60.0 g, 512 mmol) was dissolved in DMF (150 mL). 80% NaH (15.9 g, 530 mmol) in 200 mL DMF was then added slowly whilst stirring under an N_2 atmosphere. Due to the exothermic reaction the temperature rose to approximately 70 °C. The resulting green suspension was stirred at room temperature and 4-chlorobenzyl chloride (**2**) (68.0 mL, 530 mmol) was added slowly. The temperature rose to 40 °C and the color changed to brown. After 3 h stirring at room temperature under inert gas only trace amounts of indole were detected by TLC (dichloromethane/petroleum ether 50−70°, 1:1). The mixture was added to 1000 g ice water and stirred until precipitation. The crystalline product was filtered off and washed with water. After drying under vacuum for about 12 h at 25−30 °C, 120.0 g (97%) of **3** were obtained as orange-yellow crystals (m.p. 42−46 °C). − IR (KBr): $\tilde{\nu}$ = 805 cm^{-1} (phenyl), 744 cm^{-1} (12C−Cl). − ^{1}H NMR (500.13 MHz, [D$_6$]DMSO): δ = 5.42 (s, 2 H, 8-H), 6.49 (dd, ^3J = 3.2, ^4J = 0.8 Hz, 1 H, 3-H), 7.01 (m, 1 H, 6-H or 5-H), 7.09 (m, 1 H, 5-H or 6-H), 7.19 (d, ^3J = 8.5 Hz, 2 H, 10-H or 11-H), 7.36 (d, ^3J = 8.5 Hz, 2 H, 11-H or 10-H), 7.41 (d, ^3J = 8.2 Hz, 1 H, 7-H or 4-H), 7.49 (d, ^3J = 3.2 Hz, 1 H, 2-H), 7.55 (d, 1 H, 4-H or 7-H). − EI-MS: *m*/*z* (%) = 241 (61.3) [M$^+$, Cl$_1$], 204 (4.3), 125 (100) [Cl-benzyl], 89 (15.8). − $C_{15}H_{12}ClN$ (241.7): calcd. C 74.53, H 5.00, N 5.79; found C 74.42, H 5.09, N 5.72.

2-[1-(4-Chlorobenzyl)-1*H*-indol-3-yl]-2-oxoacetyl Chloride (5): Compound **3** (121.0 g, 501 mmol) was dissolved in 500 mL *tert*-butyl methyl ether and cooled to −1 °C whilst stirring under an N_2 atmosphere. Oxalyl chloride (**4**; 51.3 mL, 602 mmol) was then added slowly so that the temperature did not rise above 5 °C. After a few minutes precipitation took place. After a further 3.5 h stirring no residual **3** could be detected by TLC (dichloromethane/petroleum ether 50−70°, 1:1). The resulting yellow-orange solid was filtered off and washed with 160 mL diethyl ether. After the addition of 500 mL diethyl ether and stirring at room temperature for about 30 minutes, the product was filtered off again and washed with 160 mL diethyl ether. After drying under vacuum at 25 °C to constant weight 149.7 g (90%) of **5** were obtained as orange crystals (m.p. 131.8 °C). − IR (KBr): $\tilde{\nu}$ = 1770 cm^{-1} (16C=O); 1658 cm^{-1} (15C=O). − ^{1}H NMR (500.13 MHz, CDCl$_3$): δ = 5.37 (s, 2 H, 8-H), 7.11 (d, ^3J = 8.2 Hz, 2 H, 10-H), 7.28−7.36 (m, 4 H, 7-H, 6-H, 11-H), 7.39 (m, 1 H, 5-H), 8.20 (s, 1 H, 2-H), 8.41 (d, ^3J = 8.0 Hz, 1 H, 4-H). − ^{13}C NMR (125.77 MHz, CDCl$_3$): δ = 50.81 (C-8), 110.76 (C-3), 110.78 (C-7), 122.93 (C-4), 124.37 (C-5), 125.10 (C-6), 127.24 (C-3a), 128.36 (C-10), 129.47 (C-11), 133.20 (C-12), 134.63 (C-9), 137.00 (C-7a), 139.33 (C-2), 169.03 (C-14), 171.83 (C-13). − EI-MS: *m*/*z* (%) = 331 (1.95) [M$^+$, Cl$_2$], 303 (13.1), 268 (92.0) [M − COCl], 125 (100) [Cl-benzyl], 89(12.2). − $C_{17}H_{11}Cl_2NO_2$ (332.2): calcd. C 61.47, H 3.33, N 4.21; found C 61.40, H 3.35, N 4.16.

2-[1-(4-Chlorobenzyl)-1*H*-indol-3-yl]-2-oxo-*N*-pyridin-4-yl Acetamide (7): 4-Aminopyridine (**6**; 33.2 g, 353 mmol) was stirred in 100 mL DMF at −3 °C. A solution of **5** (50.0 g, 150 mmol) in 250 mL DMF was then added slowly so that the temperature stayed below 3 °C. This mixture was stirred at 0° to 3 °C for an additional 1−3 hours. No glyoxylic acid chloride (**5**) could be detected by TLC after that time (dichloromethane/methanol/25% ammonia, 90:10:1). Under cooling (exothermic reaction!) 100 mL demineralized water were added and a crystalline, colorless precipitate appeared. After warming to room temperature the solid was filtered off and washed thoroughly with water. The solid product was suspended in 465 mL ethanol and stirred for one hour at room temperature, filtered off and finally washed twice with 58 mL ethanol. After drying in vacuum at 50 °C, 37.7 g (64.2%) of **7** was obtained as colorless crystals (m.p. 264 °C). Recrystallisation from dichloromethane yielded thin needles which were suitable for the X-ray structure analysis. − IR (KBr): $\tilde{\nu}$ = 1688 cm^{-1}, 1631 cm^{-1} (16C=O and 15C=O). − ^{1}H NMR (500.13 MHz, [D$_6$]DMSO): δ = 5.63 (s, 2 H, 8-H), 7.33 (m, 2 H, 5-H and 6-H), 7.35 (d, ^3J = 8.5 Hz, 2 H, 10-H), 7.42 (d, ^3J = 8.5 Hz, 2 H, 11-H), 7.61 (m, 1 H, 7-H), 7.86 (dd, ^3J = 6.3, ^4J = 1.6 Hz, 2 H, 17-H), 8.31 (m, 1 H, 4-H), 8.52 (d, ^3J = 6.3, ^4J = 1.6 Hz, 2 H, 18-H), 9.01 (s, 1 H, 2-H), 11.08 (s, 1 H, H-15). − ^{13}C NMR (125.77 MHz, [D$_6$]DMSO): δ = 49.09 (C-8), 111.10 (C-3), 111.60 (C-7), 114.10 (C-17), 121.45 (C-4), 123.27 (C-5), 123.84 (C-6), 126.76 (C-3a), 128.66 (C-11), 129.22 (C-10), 132.42 (C-12), 135.53 (C-9), 136.20 (C-7a), 141.35 (C-2), 144.70 (C-16), 150.34 (C-18), 162.93 (C-14), 180.61 (C-13). − ^{1}H NMR (500.13 MHz, [D$_9$]NMP): δ = 5.80 (s, 2 H, 8-H), 7.33 (m, 1 H, 6-H), 7.34 (m, 1 H, 5-H), 7.46 (d, ^3J = 8.5 Hz, 2 H, 11-H), 7.51 (d, ^3J = 8.5 Hz, 2 H, 10-H), 7.73 (m, 1 H, 7-H), 8.02 (d, ^3J = 5.8 Hz, 2 H, 17-H), 8.35 (m, 1 H, 4-H), 8.58 (d, ^3J = 5.8 Hz, 2 H, 18-H), 9.14 (s, 1 H, 2-H), 10.99 (s, 1 H, H-15). − ^{13}C NMR (125.77 MHz, [D$_9$]NMP): δ = 50.05 (C-8), 112.12 (C-7), 112.21 (C-3), 114.72 (C-17), 122.23 (C-4), 123.74 (C-5), 124.39 (C-6), 127.91 (C-3a), 129.36 (C-11), 130.05 (C-10), 133.52 (C-12), 136.55 (C-9), 137.27 (C-7a), 142.01 (C-2), 145.72 (C-16), 151.14 (C-18), 163.65 (C-14), 181.10 (C-13). − ESI-MS: *m*/*z* (%) = 390 (100) [M + H$^+$], 362 (12) [M + H − CO], 268 (18) [M + H − (CO-NH-pyridyl)]. − $C_{22}H_{16}ClN_3O_2$ (389.84): calcd. C 67.78, H 4.14, N 10.78; found C 67.70, H 4.18, N 10.71.

X-ray Crystallographic Data for 7: $C_{22}H_{16}ClN_3O_2$, M_r = 389.84 g mol^{-1}, monoclinic, space group $P2_1/c$, a = 20.423(3), b = 5.0164(8), c = 18.119(3) Å, β = 105.766(17)°, V = 1786.4(5) Å^3, Z = 4, d_{calc} = 1.449 g cm^{-3}, μ = 2.38 cm^{-1} at −138 °C (135 K). A colorless, thin needle with dimensions 0.02 × 0.08 × 1.6 mm was measured on a SIEMENS SMART CCD diffractometer with Mo-K_α radiation (λ = 0.71073 Å). Repeatedly measured reflections remained stable. An empirical absorption correction was made using the program SADABS.[12] The correction factor ranged from 0.814 to 1.000. Equivalent reflections were averaged, resulting in 4685 unique reflections [2872 observed with $I > 2\sigma(I)$]. $R(I)_{\mathrm{int}} = 0.064$. The structure was determined by direct methods using the program SHELXS. The H atoms were taken from a difference synthesis and were refined with isotropic thermal parameters. The structure was refined on F^2 values using the program SHELXL-97[13] to give $wR2 = 0.109$, $R1[I > 2\sigma(I)] = 0.058$ and $S = 1.24$ for 318 refined parameters using all 4685 unique reflections. The final difference density was between -0.33 and $+0.32$ e A^{-3}. Crystallographic data (excluding structure factors) for **7** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-137927. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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[1] [1a] E. Günther, P. Emig, D. Reichert, G. Bacher, B. Nickel, S. Baasner, G. Le Baut, P. Marchand, ASTA Medica AG, Discovery and Synthesis of novel N-substituted Indolyl-3-glyoxylic acid derivatives with tubulin-binding activity as anticancer agents, *Poster Presentation 91st AACR Annual Meeting, April 1−5, 2000, San Francisco.* − [1b] G. Bacher, B. Nickel, A. Shandra, T. Beckers, P. Emig, T. Klenner, ASTA Medica AG, D-24851, a novel synthetic Tubulin Inhibitor, exerts superior in vivo antitumoral activity to Paclitaxel or Vincristine, efficacy against multidrug resistant tumors, and lacks Neurotoxicity, *Poster Presentation 91st AACR Annual Meeting, April 1−5, 2000, San Francisco.* − [1c] S. E. Draheim, et al. Indole inhibitors of human nonpancreatic secretory phospholipase A2. 3. Indol-3-yl-glyoxylamides, *J. Med. Chem.* **1996**, *39(26)*, 5159. − [1d] G. Domschke, H. Fürst, Notiz zur Darstellung einiger [1-Benzyl-2-methyl-5-methoxyindolyl-(3)]-glyoxylsäureamide, *Chem. Ber.* **1961**, *94*, 2353.

[2] B. Nickel, S. Szelenyi, J. Schmidt, P. Emig, D. Reichert, E. Günther, K. Brune, ASTA Medica AG, Indol-3-yl-glyoxylsäure-Derivate mit Antitumorwirkung, *WO 99/51224*.

[3] G. Le Baut, C. Menciu, B. Kutscher, P. Emig, S. Szelenyi, K. Brune, ASTA Medica AG, N-Substituted Indol-3-yl-glyoxylamids with Antiasthmatic, Antiallergic and Immunsuppressive/Immunomodulating effect, *WO98/09946*.

[4] R. Wagner, S. Berger, *J. Magn. Reson. Ser. A* **1996**, *123*, 119−121.

[5] W. Willker, D. Leibfritz, R. Kerssebaum, W. Bermel, *Magn. Reson. Chem.* **1993**, *31*, 287−292.

[6] H. Kessler, C. Griesinger, J. Zarbock, H. R. Loosli, *J. Magn. Reson.* **1984**, *57*, 331−336.

[7] B. Reif, M. Köck, R. Kerssebaum, H. Kang, W. Fenical, C. Griesinger, *J. Magn. Reson. Ser A* **1996**, *118*, 282−285.

[8] A. Bax, R. Freeman, T. A. Frenkiel, *J. Am. Chem. Soc.* **1981**, *103*, 2102−2104.

[9] [9a] E. Höhne, I. Seidel, *Krist. Tech.* **1979**, *14*, 1097−1105. − [9b] E. Höhne, I. Seidel, *Krist. Tech.* **1980**, *15*, 885−890.

[10] [10a] A. I. Yanovskii, A. E. Kalinin, Y. T. Struchkov, E. G. Bykhovskaya, I. L. Knunyants, *Zh. Strukt. Khim.* **1981**, *22*, 125−130 − [10b] J. Zuckermann-Schpector, A. da C. Pinto, J. F. M. Da Silva, R. B. Da Silva, *Acta. Cryst.* **1994**, *C50*, 87−88 − [10c] D. S. C. Black, D. C. Craig, D. B. McConnell, *J. Am. Chem. Soc.* **1996**, *118*, 8148−8149.

[11] G. R. Desiraju, T. Steiner, *The weak hydrogen bond*, Oxford University Press, **1999**.

[12] G. M. Sheldrick, (1996) SADABS. Siemens Area Detector Absorption Correction Software. University of Göttingen, Germany.

[13] G. M. Sheldrick, (1997) SHELXL-97. Program for the refinement of crystal structures. University of Göttingen, Germany.

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