Letter - spectral assignment

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^{1}H and ^{13}C NMR spectral data of *p*-nitrobenzenesulfonamides and dansylsulfonamides derived from *N*-alkylated *o*-(purinemethyl)anilines

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Introduction

In recent years, purine bases have been the subject of extensive research that led to the discovery of thousands of biological active compounds, including antineoplastic ones.[1–6] We synthesized a novel series of alkylated purines (**1-9**) with notable *in vitro* anti-proliferative activities, low toxicity and systemic distribution after oral administration *in vivo*.[1] The design of these compounds was based on the modifications of acyclic *O,N*-acetals, previously described by our research group as anti-proliferative agents.[7–10] We have also prepared the 5-fluorouracil (5-FU) derivative (**10**) as a prototype compound. Finally, the fluorescent analogous (**11-14**) of the most active compounds were synthesized in order to study the *in vitro* and *in vivo* drug distributions.[1] The *p*-nitrobenzenesulfonyl group was interchanged with the dansyl group as a chromophore because of its similarity. Moreover, a fluorescence study of some anti-tumour drugs with a dansyl [5-(dimethylamino)naphthalene-1-sulfonyl] group in their structure that present no toxicity *in vivo*[11] confirms the use of this chromophore in the design.

Although the structure of these derivatives was determined by means of standard spectroscopic techniques (^{1}H, ^{13}C NMR and MS), a detailed NMR study has been performed in order to unequivocally corroborate their structures. Herein, we report the ^{1}H and ^{13}C NMR unequivocal assignments of a series of anti-proliferative compounds. The spectra of the precursors and intermediate derivatives of the synthesis pathway for their preparation are also included.

Experimental

NMR spectroscopy was carried out at the Centro de Instrumentación Científica, Universidad de Granada (Spain), and the data were recorded at 400 MHz (^{1}H) and 100 MHz (^{13}C) on a Varian NMR System 400, or at 300 MHz (^{1}H) and 75 MHz (^{13}C) on a Varian Inova spectrometer at ambient temperature. Chemical shifts (δ) are quoted in ppm and are referenced to the residual solvent peak. Spin multiplicities are given as s (singlet), d (doublet), dd (double doublet), ddd (double double doublet), pst (pseudotriplet), t (triplet) and m (multiplet). Coupling constants (J) are given in Hz. The digital resolution of all ^{13}C spectra recorded is 0.9536 Hz/points. The following parameters were used in DEPT experiments: PW (135°), 9.0 ms; recycle time, 1 s; 1/2 J (CH) = 4 ms; 65 536 data points acquired and transformed from 1024 scans; spectral width, 15 KHz; and line broadening, 1.3 Hz. HMBC spectra were measured with a pulse sequence gc2hmbc (Standard sequence, Agilent Vnmrj_3.2A software) optimized for 8 Hz (inter-pulse delay for the evolution of long-range couplings: 62.5 ms). The HSQC spectra were measured with a pulse sequence gc2hsqcse (Standard sequence Agilent Vnmrj_3.2A software).

Results and discussion

The *N*-9-substituted derivatives (isomers **1-8**, **11**, **13**; Scheme 1) and the *N*-1-5-FU derivative **10** (Scheme 1) were obtained by microwave-assisted Mitsunobu reaction as previously reported.[1] We were also able to isolate the *N*-3-adenine derivative **9** (Scheme 1) and the *N*-7-2,6-dichloropurine derivatives **12** and **14** (Scheme 1).[1] By-products **19** and **20** (Scheme 1) were also obtained when compounds **15** and **16** were treated with tetrabutylammonium fluoride.

^{1}H NMR and ^{13}C NMR data (chemical shifts, multiplicity and coupling constants) for compounds **1-25** are shown in Tables 1–14. Unambiguous assignments for all NMR signals were made through the combined information of one-dimensional and two-dimensional NMR experiments such as DEPT, HSQC and HMBC (see Supporting information).

The procedure used to determine the structures of **1-25** from their NMR data is as follows: The identification of *N*-9-substituted derivatives **1-7** relies on the observation of the correlation of the benzylic hydrogen atoms linked to the purine with the C-4 of the purine moiety in the HMBC spectrum. The C-4 of the purine moiety (C-4$_{pur}$) can be identified because of its 1,3-relationship with the benzylic hydrogen atoms in **1-7** and in addition the H-2 atom of the purine ring in **1**, **2**, **4-6** (Fig. 1).

The link between the benzylic hydrogen atoms and the quaternary carbons of the 2,6-dichloropurine moiety C-4$_{pur}$ and C-5$_{pur}$

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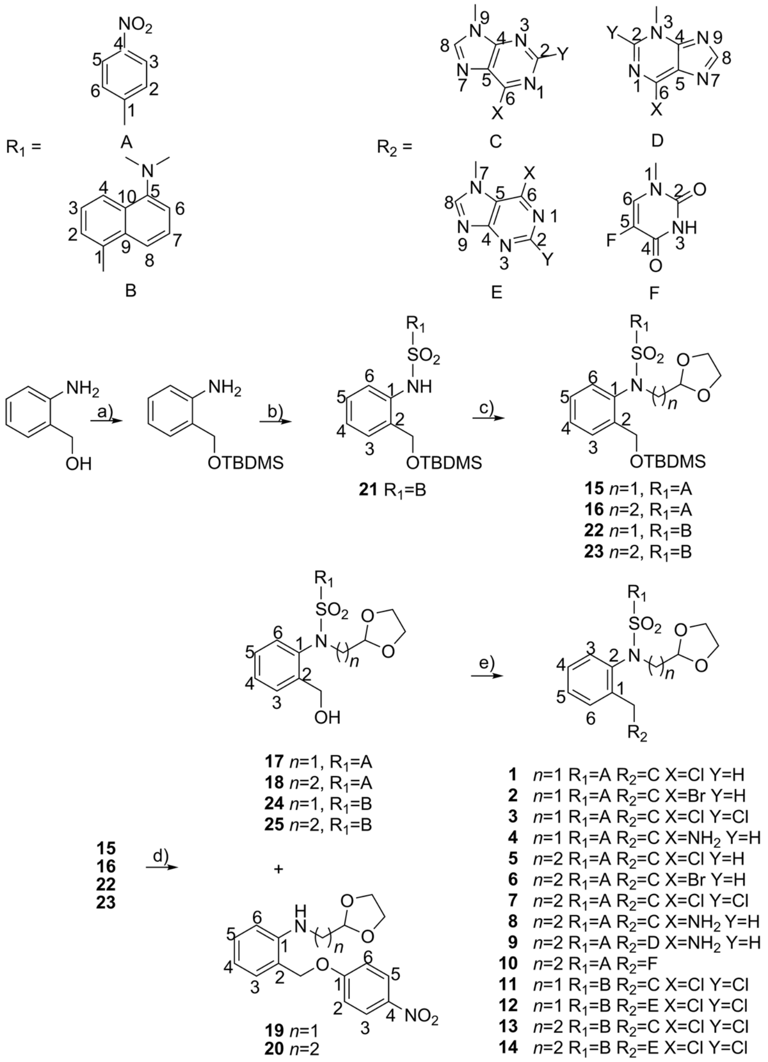


Scheme 1. Reagents and conditions: a) *tert*-Butyldimethylsilyl choride (TBDMS-Cl), 4-(dimethylamino)pyridine (DMAP), triethylamine (Et_3N), anhydrous dichloromethane (CH_2Cl_2). b) *p*-Nitrobenzenesulfonyl chloride (pNO_2-C_6H_4-SO_2Cl), anhydrous CH_2Cl_2; dansyl chloride, Et_3N, anhydrous CH_2Cl_2 (for **21**). c) 2-Hydroxymethyl-1,3-dioxolane (for **15** and **22**) or 2-(2-hydroxyethyl)-1,3-dioxolane (for **16** and **23**), diisopropylazodicarboxylate (DIAD), triphenylphosphine (PPh_3), anhydrous tetrahydrofurane (THF). d) TBAF, anhydrous THF. e) DIAD, PPh_3, anhydrous THF, microwave irradiation.

allows us to distinguish the *N*-9-substituted from the *N*-7-substituted dansyl derivatives (**11**, **13** from **12**, **14**, respectively). The distinction between the C-4$_{pur}$ and C-5$_{pur}$ signals in the spectrum is based on previously reported data of *N*-7-alkylated and *N*-9-alkylated purines.[12,13] C-4$_{pur}$ is correlated with the benzylic hydrogen atoms in the *N*-9 isomers, while C-5$_{pur}$ is correlated with the benzylic hydrogen atoms in the *N*-7 isomers (Fig. 2).

The discrimination between the *N*-9-substituted and *N*-3-substituted derivatives of adenine (**8** and **9**, respectively) relies on the interaction between the benzylic hydrogen atoms and C-2, C-4 and C-8 atoms of the adenine moiety (Fig. 3). While the benzylic hydrogen atoms are correlated with C-4$_{pur}$ and C-8$_{pur}$ in the *N*-9 regioisomer **8**, the benzylic hydrogen atoms are correlated with C-2$_{pur}$ and C-4$_{pur}$ in the *N*-3 regioisomer **9** (Fig. 3). Moreover, the 1,3-relationships between the H-8$_{pur}$ (for **8**) and the H-2$_{pur}$ (for **9**) with the benzylic carbon atom (Fig. 3) are observed.

The identification of the *N*-1-5-FU regioisomer **10** relies on the 1,3-relationship between the benzylic hydrogen atoms linked to the 5-FU and the C-6 of 5-FU moiety, and vice versa, the H-6 of 5-FU moiety and the benzylic carbon (Fig. 4).

Some variations are found in the chemical shifts between compounds **15-18** and **19-20**. H-3,5$_{PhNO2}$ and H-2,6$_{PhNO2}$ resonate at a higher field in **15-18** (δ 7.83–8.35 ppm) than in **19-20** (δ 7.08–8.22 ppm). The reverse trend is observed in the case of the benzylic hydrogen atoms where the signals appear at a higher field in **15-18** than in **19-20** (Table 4). The same tendency is shown in their ^{13}C spectra (Table 12).

Adenine derivatives (**4**, **8**, **9**) exhibit different characteristics in their ^1H spectra in relation to those of the purines **1-3**, **5-7**. Pronounced downfield shifts are observed (Table 1) for H-2$_{pur}$ (δ 8.38–8.44 ppm) and H-8$_{pur}$ (δ 8.04–8.13 ppm) signals for the adenine isomers compared with the corresponding signals for purines **1-3**, **5-7** (δ 8.72–8.80 ppm for H-2$_{pur}$, 8.34–8.42 ppm for H-8$_{pur}$).

The ^{13}C NMR signals for C-4$_{5FU}$, C-5$_{5FU}$ and C-6$_{5FU}$ in **10** should be highlighted. The ^1J (F,C) and ^2J (F,C) give rise to the doublet appearance of the signals (Table 9).

Table 1. ^1H NMR data for **1-9** (δ, ppm; *J*, Hz)

	H-2_{pur}	H-8_{pur}	H-3, 5_{PhNO2}	H-2, 6_{PhNO2}	H-3_{Ph}	H-4_{Ph}	H-5_{Ph}	H-6_{Ph}	*N*H_{2pur}	Ph-CH_2	*N*-CH_2	*N*-CH_2-$C\underline{H_2}$	CH_{2diox}	CH_{diox}
1	8.80 (s)	8.38 (s)	8.35 (d, 8.8)	7.84 (d, 8.8)	6.49 (d, 7.3)	7.21–7.17 (m)	7.29–7.25 (m)	7.05 (d, 7.3)		5.92 (d, 16.2) 5.85 (d, 16.2)	4.16–4.04 (m) 3.30 (dd, 13.9, 5.6)		4.01–3.82 (m)	5.18–5.15 (m)
2	8.75 (s)	8.38 (s)	8.35 (d, 8.7)	7.84 (d, 8.7)	6.45 (d, 7.7)	7.20–7.17 (m)	7.28–7.25 (m)	7.05 (d, 7.7)		5.92 (d, 16.1) 5.84 (d, 16.1)	4.09 (dd, 14.1, 4.0) 3.30 (dd, 14.1, 5.6)		4.00–3.83 (m)	5.16 (dd, 5.6, 4.3)
3		8.34 (s)	8.38 (d, 8.9)	7.84 (d, 8.9)	6.47 (dd, 7.6, 1.3)	7.20 (ddd, 7.8, 7.6, 1.4)	7.30 (ddd, 7.8, 7.6, 1.3)	6.80 (dd, 7.6, 1.4)		5.90 (d, 16.2) 5.80 (d, 16.2)	4.09 (dd, 13.8, 4.4) 3.28 (dd, 13.8, 5.6)		4.00–3.86 (m)	5.15 (dd, 6.0, 4.1)
4	8.42 (s)	8.04 (s)	8.37 (d, 8.8)	7.86 (d, 8.8)	6.44 (d, 7.9)	7.17–7.14 (m)	7.28–7.25 (m)	7.07 (d, 7.9)	5.98 (s)	5.82 (d, 16.2) 5.77 (d, 16.2)	4.09 (dd, 13.8, 4.3) 3.33 (dd, 13.8, 5.5)		4.01–3.85 (m)	5.17 (pst, 4.9)
5	8.78 (s)	8.38 (s)	8.38 (d, 8.9)	7.85 (d, 8.9)	6.49 (dd, 7.7, 1.3)	7.21 (ddd, 7.7, 7.7, 1.3)	7.31–7.25 (m)	6.41 (dd, 7.7, 1.3)		5.89 (d, 16.2) 5.79 (d, 16.2)	4.26–4.07 (m) 3.41–3.28 (m)	2.07–1.95 (m) 1.89–1.75 (m)	3.99–3.77 (m)	4.92 (pst, 4.1)
6	8.72 (s)	8.42 (s)	8.37 (d, 8.8)	7.84 (d, 8.8)	6.48 (d, 7.3)	7.19 (pst, 7.3)	7.27 (pst, 7.3)	7.05 (d, 7.3)		5.87 (d, 16.1) 5.78 (d, 16.1)	4.24–4.08 (m) 3.40–3.25 (m)	2.08–1.94 (m) 1.87–1.74 (m)	4.00–3.75 (m)	4.90 (pst, 4.0)
7		8.39 (s)	8.36 (d, 8.5)	7.85 (d, 8.5)	6.48 (d, 7.5)	7.22 (pst, 7.5)	7.30 (pst, 7.5)	7.06 (d, 7.5)		5.80 (d, 16.0) 5.70 (d, 16.0)	4.21–4.09 (m) 3.33–3.21 (m)	2.04–1.93 (m) 1.84–1.71 (m)	3.97–3.72 (m)	4.93 (pst, 3.8)
8	8.38 (s)	8.04 (s)	8.36 (d, 8.8)	7.86 (d, 8.8)	6.45 (d, 7.9)	7.19–7.15 (m)	7.28–7.25 (m)	7.07 (d, 7.9)		5.75 (d, 16.2) 5.71 (d, 16.2)	4.21–4.14 (m) 3.40–3.28 (m)	2.07–1.99 (m) 1.86–1.75 (m)	3.99–3.77 (m)	4.91 (pst, 4.1)
9	8.44 (s)	8.13 (s)	8.38 (d, 8.8)	7.85 (d, 8.8)	6.47 (d, 7.7)	7.25–7.20 (m)	7.33–7.29 (m)	7.13 (d, 7.7)		6.05 (d, 15.8) 5.88 (d, 15.8)	4.29–4.11 (m) 3.41–3.24 (m)	2.04–1.90 (m) 1.90–1.74 (m)	4.03–3.73 (m)	4.90 (pst, 3.9)

Multiplicity and coupling constants are given in parentheses. ^1H shift assignments are in agreement with the HSQC and HMBC spectra. $CDCl_3$ was used as solvent in the NMR experiments for all compounds.

Table 2. ^{1}H NMR data for **10** (δ, ppm; J, Hz)

	H-3$_{5FU}$	H-6$_{5FU}$	H-3,5$_{PhNO2}$	H-2,6$_{PhNO2}$	H-3$_{Ph}$	H-4$_{Ph}$	H-5$_{Ph}$	H-6$_{Ph}$	Ph-CH$_2$	N-CH$_2$	N-CH$_2$-$\underline{\mathrm{CH_2}}$	CH$_{2diox}$	CH$_{diox}$
10	8.85 (d, 5.0)	7.62 (d, 5.0)	8.38 (d, 8.8)	7.86 (d, 8.8)	6.44 (d, 7.9)	7.24–7.19 (m)	7.43–7.38 (m)	7.28 (d, 7.2)	5.45 (d, 16.0) 5.09 (d, 16.0)	4.20–4.02 (m) 3.35–3.23 (m)	2.04–1.87 (m) 1.79–1.72 (m)	3.99–3.74 (m)	4.88 (pst, 4.1)

Multiplicity and coupling constants are given in parentheses. ^{1}H shift assignments are in agreement with the HSQC and HMBC spectra. CDCl$_3$ was used as solvent in the NMR experiment.

Table 3. ^{1}H NMR data for **11-14** (δ, ppm; J, Hz)

	H-4$_{dan}$	H-8$_{dan}$	H-2$_{dan}$	H-7$_{dan}$	H-3$_{dan}$	H-6$_{dan}$	H-8$_{pur}$	H-3$_{Ph}$	H-4$_{Ph}$	H-5$_{Ph}$	H-6$_{Ph}$	Ph-CH$_2$	N-CH$_2$	N-CH$_2$-$\underline{\mathrm{CH_2}}$	CH$_{2dio}$	CH$_{diox}$	N(CH$_3$)$_2$
11	8.60 (d, 7.6)	8.01 (d, 7.6)	8.06 (dd, 7.6, 1.2)	7.32 (pst, 7.6)	7.48 (pst, 7.6)	7.14 (d, 7.6)	8.34 (s)	6.36 (d, 7.8)	6.95–6.91 (m)	7.19–7.15 (m)	6.99 (d, 7.8)	5.92 (d, 16.1) 5.82 (d, 16.1)	4.24 (dd, 13.9, 4.5) 3.26 (dd, 13.9, 5.5)		4.03–3.82 (m)	5.18 (pst, 5.0)	2.89 (s)
12	8.60 (d, 8.4)	8.01 (d, 8.7)	8.05 (dd, 7.5, 1.1)	7.33 (dd, 8.7, 7.6)	7.49 (dd, 8.4, 7.5)	7.14 (d, 7.6)	8.31 (s)	6.74 (d, 8.0)	7.01–6.95 (m)	7.22–7.14 (m)	6.43 (d, 8.0)	6.12 (s)	4.20 (dd, 14.0, 4.3) 3.22 (dd, 14.0, 5.9)		4.02–3.76 (m)	5.17 (dd, 5.8, 4.3)	2.89 (s)
13	8.58 (d, 8.5)	8.09–8.06 (m)	8.09–8.06 (m)	7.33 (dd, 8.7, 7.5)	7.49 (dd, 8.5, 7.5)	7.13 (d, 7.5)	8.27 (s)	6.49 (dd, 8.4, 1.0)	7.01–6.97 (m)	7.22–7.17 (m)	7.01–6.97 (m)	5.79 (d, 15.9) 5.73 (d, 15.9)	4.21–4.09 (m) 3.47–3.39 (m)	1.99–1.90 (m) 1.82–1.73 (m)	3.95–3.76 (m)	4.89 (pst, 4.1)	2.88 (s)
14	8.59 (d, 8.4)	8.06 (d, 8.5)	8.06 (d, 7.9)	7.34 (dd, 8.5, 7.6)	7.49 (dd, 8.4, 7.9)	7.13 (d, 7.6)	8.28 (s)	6.56 (d, 7.6)	7.03 (pst, 7.6)	7.21 (pst, 7.6)	6.68 (d, 7.6)	6.07 (d, 16.7) 5.94 (d, 16.7)	4.15–4.04 (m) 3.51–3.41 (m)	1.96–1.85 (m) 1.84–1.74 (m)	3.94–3.74 (m)	4.88 (pst, 4.1)	2.89 (s)

Multiplicity and coupling constants are given in parentheses. ^{1}H shift assignments are in agreement with the HSQC and HMBC spectra. CDCl$_3$ was used as solvent in the NMR experiments for all compounds.

Table 4. ^{1}H NMR data for **15-20** (δ, ppm; *J*, Hz)

	H-3,5 PhNO2	H-2,6 PhNO2	$H\text{-}3_{Ph}$	$H\text{-}4_{Ph}$	$H\text{-}5_{Ph}$	$H\text{-}6_{Ph}$	Ph-CH_2	*N*H	*N*-CH_2	*N*-CH_2-$\underline{CH_2}$	CH_{2diox}	CH_{diox}	$C\underline{H}_3$-C-Si	CH_3-Si
15	8.33 (d, 9.0)	7.85 (d, 9.0)	7.69 (dd, 7.7, 1.1)	7.39 (ddd, 7.7, 7.4, 1.1)	7.11 (ddd, 7.8, 7.4, 1.1)	6.47 (dd, 7.8, 1.1)	5.02 (d, 14.4) 4.94 (d, 14.4)		3.91 (dd, 14.1, 5.1) 3.48 (dd, 14.1, 5.1)		3.89–3.77 (m)	4.96 (pst, 4.7)	0.97 (s)	0.12 (s)
16	8.32 (d, 8.6)	7.84 (d, 8.6)	7.66 (d, 7.5)	7.35 (pst, 7.5)	7.10 (pst, 7.5)	6.43 (d, 7.5)	4.94 (d, 14.3) 4.87 (d, 14.3)		4.03–3.92 (m) 3.43–3.30 (m)	2.03–1.89 (m) 1.80–1.65 (m)	3.92–3.75 (m)	4.80 (pst, 4.4)	0.92 (s)	0.02 (s)
17	8.34 (d, 9.0)	7.83 (d, 9.0)	7.64 (dd, 7.6, 1.5)	7.40 (ddd, 7.6, 7.5, 1.2)	7.17 (ddd, 7.6, 7.5, 1.5)	6.40 (dd, 7.6, 1.2)	4.93 (d, 12.5) 4.75 (d, 12.5)		3.98 (dd, 14.0, 4.1) 3.32 (dd, 14.0, 5.7)		3.95–3.80 (m)	5.07 (dd, 5.6, 4.1)		
18	8.35 (d, 8.8)	7.84 (d, 8.8)	7.67 (d, 7.7)	7.41 (pst, 7.7)	7.18 (pst, 7.7)	6.41 (d, 7.7)	4.84 (d, 12.6) 4.63 (dd, 12.6, 7.4)		4.05–3.96 (m) 3.35–3.23 (m)	1.96–1.83 (m) 1.72–1.60 (m)	3.91–3.71 (m)	4.80 (pst, 4.2)		
19	8.21 (d, 9.3)	7.08 (d, 9.3)	7.21 (dd, 7.7,1.6)	6.80–6.72 (m)	7.28 (ddd, 7.8, 7.6, 1.6)	6.80–6.72 (m)	5.14 (s)	4.62 (s)	3.39 (d, 3.8)		3.97–3.86 (m)	5.15–5.11 (m)		
20	8.22 (d, 9.2)	7.08 (d, 9.2)	7.21 (dd, 7.3, 1.3)	6.75–6.72 (m)	7.30 (ddd, 7.9, 7.6, 1.3)	6.75–6.72 (m)	5.14 (s)	4.97 (s)	3.31 (t, 6.2)	2.07–1.99 (m)	3.91–3.63 (m)	4.95 (t, 4.4)		

Multiplicity and coupling constants are given in parentheses. ^{1}H shift assignments are in agreement with the HSQC and HMBC spectra. $CDCl_3$ was used as solvent in the NMR experiments for all compounds.

Table 5. ^{1}H NMR data for **21** (δ, ppm; J, Hz)

	H-4$_{dan}$	H-8$_{dan}$	H-2$_{dan}$	H-7$_{dan}$	H-3$_{dan}$	H-6$_{dan}$	H-6$_{Ph}$	H-5$_{Ph}$	H-4$_{Ph}$	H-3$_{Ph}$	*N*H	Ph-CH$_2$	*N*(CH$_3$)$_2$	C$\underline{H_3}$-C-Si	CH$_3$-Si
21	8.49 (d, 8.5)	8.39 (d, 8.7)	8.22 (dd, 7.3, 1.2)	7.53 (dd, 8.7, 7.7)	7.47–7.42 (m)	7.18–7.14 (m)	7.47–7.42 (m)	7.18–7.14 (m)	6.93 (ddd, 7.5, 7.4, 1.1)	6.88 (dd, 7.5, 1.4)	8.66 (s)	4.30 (s)	2.86 (s)	0.94 (s)	0.06 (s)

Multiplicity and coupling constants are given in parentheses. ^{1}H shift assignments are in agreement with the HSQC and HMBC spectra. CDCl$_3$ was used as solvent in the NMR experiment.

Table 6. ^{1}H NMR data of the aromatic groups for **22-25** (δ, ppm; J, Hz)

	H-4$_{dan}$	H-8$_{dan}$	H-2$_{dan}$	H-7$_{dan}$	H-3$_{dan}$	H-6$_{dan}$	H-6$_{Ph}$	H-5$_{Ph}$	H-4$_{Ph}$	H-3$_{Ph}$
22	8.54 (d, 8.4)	8.15 (d, 8.7)	8.02 (dd, 7.5, 1.1)	7.36 (dd, 8.7, 7.6)	7.42 (dd, 8.4, 7.5)	7.14 (d, 7.6)	6.64 (d, 7.9)	6.96 (ddd, 7.9, 7.5, 1.2)	7.30–7.26 (m)	7.56 (d, 7.7)
23	8.54 (d, 8.5)	8.17 (d, 8.7)	8.05 (dd, 7.5, 1.2)	7.38 (dd, 8.7, 7.5)	7.44 (dd, 8.5, 7.5)	7.14 (d, 7.5)	6.67 (dd, 8.0, 0.8)	7.00 (ddd, 8.0, 7.6, 1.5)	7.29 (ddd, 7.6, 7.4, 1.1)	7.56 (d, 7.4)
24	8.57 (d, 8.4)	8.05–8.02 (m)	8.05–8.02 (m)	7.32 (dd, 8.6, 7.6)	7.45 (dd, 8.4, 7.5)	7.14 (d, 7.6)	6.31 (dd, 8.0, 0.8)	6.92 (ddd, 8.0, 7.5, 1.7)	7.29 (ddd, 7.7, 7.5, 0.8)	7.57 (dd, 7.7, 1.5)
25	8.56 (d, 8.4)	8.08 (d, 8.7)	8.05 (dd, 7.5, 1.1)	7.34 (dd, 8.7, 7.6)	7.46 (dd, 8.4, 7.5)	7.14 (d, 7.6)	6.37 (dd, 7.9, 0.8)	6.95 (ddd, 7.9, 7.5, 1.5)	7.30 (ddd, 7.6, 7.5, 0.8)	7.60 (dd, 7.6, 1.5)

Multiplicity and coupling constants are given in parentheses. ^{1}H shift assignments are in agreement with the HSQC and HMBC spectra. CDCl$_3$ was used as solvent in the NMR experiments for all compounds.

Table 7. ^{1}H NMR data of the remaining signals for **22-25** (δ, ppm; *J*, Hz)

	Ph-CH$_2$	*N*-CH$_2$	*N*(CH$_3$)$_2$	*N*-CH$_2$-$\underline{\text{CH}_2}$	$\underline{\text{CH}_3}$-C-Si	CH$_3$-Si
22	4.85 (d, 14.4) 4.57 (d, 14.4)	3.95 (dd, 14.1, 4.9) 3.51 (dd, 14.1, 4.6)	2.88 (s)		0.92 (s)	0.02 (s)
23	4.71 (d, 14.1) 4.58 (d, 14.1)	3.95–3.88 (m) 3.64–3.53 (m)	2.88 (s)	1.95–1.86 (m) 1.81–1.73 (m)	0.90 (s)	0.02 (s)
24	4.92 (dd, 12.4, 5.2) 4.70 (dd, 12.4, 5.3)	4.15 (dd, 14.1, 4.3) 3.25 (dd, 14.1, 5.5)	2.88 (s)			
25	4.89 (d, 12.3) 4.62–4.53 (m)	4.14–4.02 (m) 3.45–3.36 (m)	2.89 (s)	1.95–1.85 (m) 1.73–1.62 (m)		

Multiplicity and coupling constants are given in parentheses. ^{1}H shift assignments are in agreement with the HSQC and HMBC spectra. CDCl$_3$ was used as solvent in the NMR experiments for all compounds.

Table 8. ^{13}C NMR data for **1-9** (δ, ppm)

	C-4$_{\text{pur}}$	C-2$_{\text{pur}}$	C-6$_{\text{pur}}$	C-8$_{\text{pur}}$	C-5$_{\text{pur}}$	C-4$_{\text{PhNO2}}$	C-1$_{\text{PhNO2}}$	C-2$_{\text{Ph}}$	C-1$_{\text{Ph}}$	C-2,6$_{\text{PhNO2}}$	C-3$_{\text{Ph}}$	C-4$_{\text{Ph}}$	C-5$_{\text{Ph}}$	C-6$_{\text{Ph}}$	C-3,5$_{\text{PhNO2}}$	Ph-CH$_2$	*N*-CH$_2$	*N*-CH$_2$ -$\underline{\text{CH}_2}$	CH$_{2\text{diox}}$	CH$_{\text{diox}}$
1	152.69	152.35	151.23	146.49	131.47	150.64	142.77	137.64	137.98	129.56	127.31	129.30	129.92	129.14	124.41	43.41	54.92		65.33	101.88
2	151.48	152.34	153.37	146.37	134.09	150.41	142.77	137.66	138.00	129.58	127.30	129.33	129.95	129.19	124.43	43.59	55.16		65.25	101.96
3	153.97	153.36	151.99	147.21	130.67	150.68	142.71	137.71	137.56	129.56	127.32	129.49	130.01	129.10	124.46	43.75	55.19		65.28	101.85
4	152.40	152.41	155.08	150.64	137.37	150.65	142.13	138.76	138.13	129.58	127.30	129.25	129.91	128.97	124.39	43.09	55.13		65.28	101.89
5	152.52	152.48	151.35	146.28	131.12	150.67	142.73	136.93	137.70	129.65	126.99	129.44	129.86	129.23	124.42	43.93	47.58	32.44	65.25	102.06
6	151.28	152.52	151.20	146.13	134.11	150.64	142.60	136.99	137.35	129.70	126.98	129.65	129.86	129.59	124.43	44.12	47.47	32.38	65.24	102.00
7	153.86	153.39	152.05	146.95	131.51	150.64	142.62	136.90	137.31	129.90	126.98	129.61	130.71	129.19	124.43	43.90	47.33	32.22	65.25	101.98
8	150.72	152.95	155.56	141.57	119.15	150.54	142.93	136.55	138.51	129.59	126.88	129.28	129.79	129.05	124.38	43.19	47.54	32.42	65.20	102.00
9	149.80	146.09	154.43	148.90	119.15	150.80	142.42	137.11	136.62	129.74	127.03	129.67	129.98	129.20	124.45	49.36	47.47	32.21	65.24	101.96

^{13}C shift assignments are in agreement with the HSQC and HMBC spectra. CDCl$_3$ was used as solvent in the NMR experiments for all compounds.

Table 9. ^{13}C NMR data for **10** (δ, ppm)

	C-4$_{5FU}$	C-2$_{5FU}$	C-5$_{5FU}$	C-6$_{5FU}$	C-4$_{PhNO2}$	C-1$_{PhNO2}$	C-2$_{Ph}$	C-1$_{Ph}$	C-2,6$_{PhNO2}$	C-3$_{Ph}$	C-4$_{Ph}$	C-5$_{Ph}$	C-6$_{Ph}$	C-3,5$_{PhNO2}$	Ph-CH$_2$	*N*-CH$_2$	*N*-CH$_2$-$\underline{\text{C}}$H$_2$	CH$_{2diox}$	CH$_{diox}$
10	157.05 (d, 26.5)	150.13	141.74 (d, 238.2)	129.12 (d, 32.9)	150.61	142.79	137.13	137.66	129.41	127.11	129.15	130.02	129.29	124.44	47.46	47.55	32.32	65.19	101.90

^{13}C shift assignments are in agreement with the HSQC and HMBC spectra. CDCl$_3$ was used as solvent in the NMR experiment

Table 10. ^{13}C NMR data of the purine and dansyl groups for **11-14** (δ, ppm)

	C-5$_{dan}$	C-1$_{dan}$	C-4$_{dan}$	C-9$_{dan}$	C-2$_{dan}$	C-10$_{dan}$	C-7$_{dan}$	C-3$_{dan}$	C-8$_{dan}$	C-6$_{dan}$	C-4$_{pur}$	C-2$_{pur}$	C-6$_{pur}$	C-8$_{pur}$	C-5$_{pur}$
11	151.80	133.19	131.34	130.65	131.50	130.11	127.89	123.25	120.03	115.51	154.07	153.24	156.33	147.51	130.59
12	151.76	132.94	131.48	130.60	131.62	130.12	128.26	123.25	119.94	115.54	163.52	144.00	153.29	151.65	122.58
13	151.85	133.34	131.22	130.54	131.50	130.08	128.10	123.28	120.01	115.45	153.92	151.74	153.22	147.12	130.66
14	151.84	133.18	131.37	130.62	131.59	130.13	128.18	123.29	119.93	115.50	163.67	144.00	153.44	151.47	122.40

^{13}C shift assignments are in agreement with the HSQC and HMBC spectra. CDCl$_3$ was used as solvent in the NMR experiment

Table 11. ^{13}C NMR data of the remaining signals for **11-14** (δ, ppm)

	C-2$_{Ph}$	C-1$_{Ph}$	C-3$_{Ph}$	C-4$_{Ph}$	C-5$_{Ph}$	C-6$_{Ph}$	Ph-CH$_2$	N(CH$_3$)$_2$	N-CH$_2$	N-CH$_2$-$\underline{\text{CH}_2}$	CH$_{2diox}$	CH$_{diox}$
11	138.18	137.52	128.47	128.91	129.26	128.19	43.90	45.57	55.04		65.14	102.46
12	138.08	137.75	129.14	128.97	129.40	127.30	45.56	46.98	55.16		65.25	101.96
13	137.21	137.00	129.12	128.63	129.24	129.04	43.93	45.55	47.14	32.66	65.16	102.20
14	137.24	137.14	129.41	129.07	129.45	127.30	47.32	45.56	47.15	32.94	65.20	102.16

^{13}C shift assignments are in agreement with the HSQC and HMBC spectra. CDCl$_3$ was used as solvent in the NMR experiment

Table 12. ^{13}C NMR data for **15-20** (δ, ppm)

	C-4$_{PhNO2}$	C-1$_{PhNO2}$	C-2$_{Ph}$	C-1$_{Ph}$	C-2,6$_{PhNO2}$	C-3$_{Ph}$	C-4$_{Ph}$	C-5$_{Ph}$	C-6$_{Ph}$	C-3,5$_{PhNO2}$	Ph-CH$_2$	N-CH$_2$	N-CH$_2$-$\underline{\text{CH}_2}$	CH$_{2diox}$	CH$_{diox}$	$\underline{\text{CH}_3}$-C-Si	C-Si	CH$_3$-Si
15	150.32	144.27	143.35	135.88	129.55	129.40	128.46	127.57	127.37	124.05	61.21	54.76		65.14	101.70	26.06	18.71	−5.06
16	150.41	144.08	143.43	135.38	129.51	129.38	128.77	127.64	126.93	124.31	61.37	47.66	32.77	65.18	102.11	26.20	18.62	−5.07
17	150.50	143.36	142.81	137.50	129.58	131.99	129.90	128.86	127.26	124.27	61.30	55.17		65.18	102.06			
18	150.28	143.28	142.78	136.38	129.50	131.73	129.75	128.87	126.75	124.32	61.08	47.63	32.42	65.16	102.02			
19	163.44	142.02	119.83	147.45	115.23	130.68	117.56	130.41	111.65	126.02	70.46	46.44		65.44	102.41			
20	163.84	141.87	119.35	147.65	115.09	130.76	116.89	130.51	111.05	125.99	70.15	39.09	33.00	64.96	104.14			

^{13}C shift assignments are in agreement with the HSQC and HMBC spectra. CDCl$_3$ was used as solvent in the NMR experiments for all compounds.

Table 13. ^{13}C NMR data for the purine and dansyl groups of **21-25** (δ, ppm)

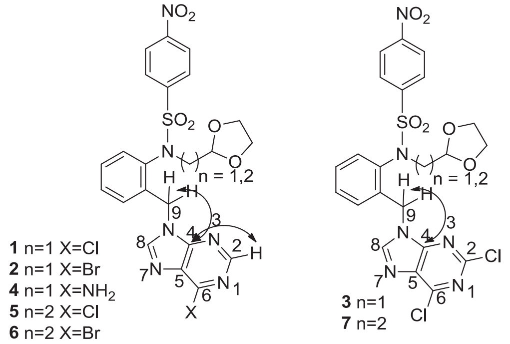
	C-5$_{dan}$	C-1$_{dan}$	C-4$_{dan}$	C-9$_{dan}$	C-2$_{dan}$	C-10$_{dan}$	C-7$_{dan}$	C-3$_{dan}$	C-8$_{dan}$	C-6$_{dan}$	C-1$_{Ph}$	C-2$_{Ph}$	C-5$_{Ph}$	C-3$_{Ph}$	C-4$_{Ph}$	C-6$_{Ph}$
21	152.03	135.57	130.68	129.97	129.95	129.74	128.36	123.26	118.95	115.31	137.26	130.38	128.78	128.00	124.22	121.46
22	151.47	134.41	130.67	130.55	131.14	129.98	127.88	123.21	120.46	115.32	136.22	143.00	126.93	127.64	128.63	129.51
23	151.60	134.66	130.60	130.52	131.13	130.06	128.07	123.30	120.50	115.34	135.53	142.90	127.15	127.88	128.66	129.49
24	151.59	133.64	130.99	130.61	131.39	130.05	128.00	123.22	120.34	115.40	138.03	142.86	128.36	131.42	129.17	128.80
25	151.63	133.87	130.85	130.52	131.27	130.06	127.94	123.27	120.33	115.37	136.69	142.62	128.36	131.29	129.11	128.82

^{13}C shift assignments are in agreement with the HSQC and HMBC spectra. CDCl$_3$ was used as solvent in the NMR experiments for all compounds

Table 14. ^{13}C NMR data of the remaining signals for **21-25** (δ, ppm)

	Ph-CH$_2$	*N*-CH$_2$	*N*-CH$_2$-$\underline{CH}_2$	CH$_{2diox}$	CH$_{diox}$	*N*(CH$_3$)$_2$	$\underline{C}$H$_3$-C-Si	C-Si	CH$_3$-Si
21	65.40					45.56	25.94	18.33	−5.26
22	61.10	54.58		64.98	102.20	45.54	26.08	18.43	−5.31
23	61.22	47.20	33.01	65.01	102.34	45.59	26.10	16.46	−5.26
24	61.53	55.07		65.03	102.54	45.57			
25	61.22	47.44	32.75	65.05	102.26	45.57			

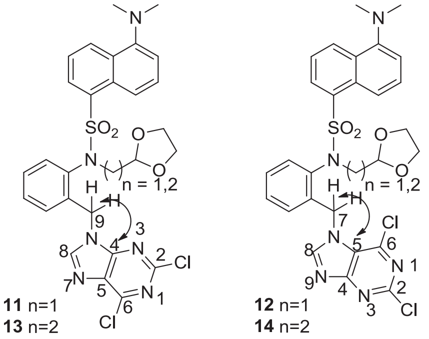
^{13}C shift assignments are in agreement with the HSQC and HMBC spectra. CDCl$_3$ was used as solvent in the NMR experiments for all compounds.



1 n=1 X=Cl
2 n=1 X=Br
4 n=1 X=NH$_2$
5 n=2 X=Cl
6 n=2 X=Br

3 n=1
7 n=2

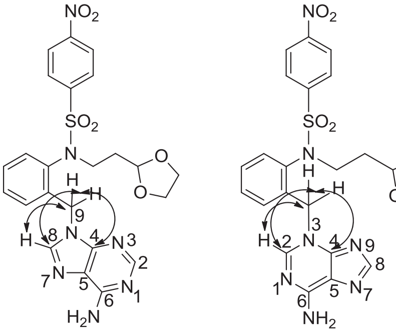
Figure 1. The HMBC interactions in the *N*-9 regioisomers **1-7**.



11 n=1
13 n=2

12 n=1
14 n=2

Figure 2. The HMBC interactions in the *N*-9 (**11**, **13**) and *N*-7 (**12**, **14**) dansyl derivatives.



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9

Figure 3. The HMBC interactions in the *N*-9 (**8**) and *N*-3 (**9**) adenine regioisomers.

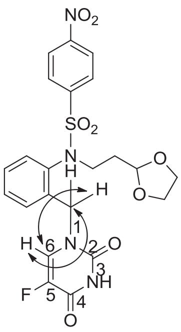

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Figure 4. The HMBC interactions in the *N*-1-5-FU (**10**) regioisomer.

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