Synthesis and Irradiation of Vitamin-B_{12}-Derived Complexes Incorporating Peripheral G·C Base Pairs

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The vitamin-B_{12} derivative **11**, incorporating a peripheral N^4-acetylcytosine moiety, was alkylated under reductive conditions with 2-(iodomethyl)-2-methylmonothiomalonate **8** bearing the complementary guanine moiety. The reaction yielded a mixture of vitamin-B_{12}-derived complexes with variations in the cytosine moiety: products **16**–**18** with a cytosine, a N^4-acetylated cytosine, and a N^4-acetylated reduced cytosine moiety were formed (see *Scheme 5*). The complexes were photolyzed in $CHCl_3$/MeCN to yield the dimethylmalonate derivative **22** (*Scheme 6*) but not the rearranged succinate, in contrast to the results obtained earlier with complexes incorporating the A·T base pair (see *Scheme 1*).

Introduction. – The mechanism of the vitamin-B_{12}-dependent methylmalonyl-succinyl rearrangement (*Scheme 1*) continues to be a challenging problem since the electronic nature of the 1,2-migration of the thioester moiety has not yet been elucidated. Proposed mechanisms include a direct radical rearrangement, a fragmentation pathway, as well as a rearrangement *via* a carbanion or *via* an organocobalt intermediate [1–6]. Furthermore, the role of the Co-atom in the rearrangement step could not be established in an irrefutable way. Model studies have shown that anionic rearrangements take place, and that radical processes are not favorable [7–12].

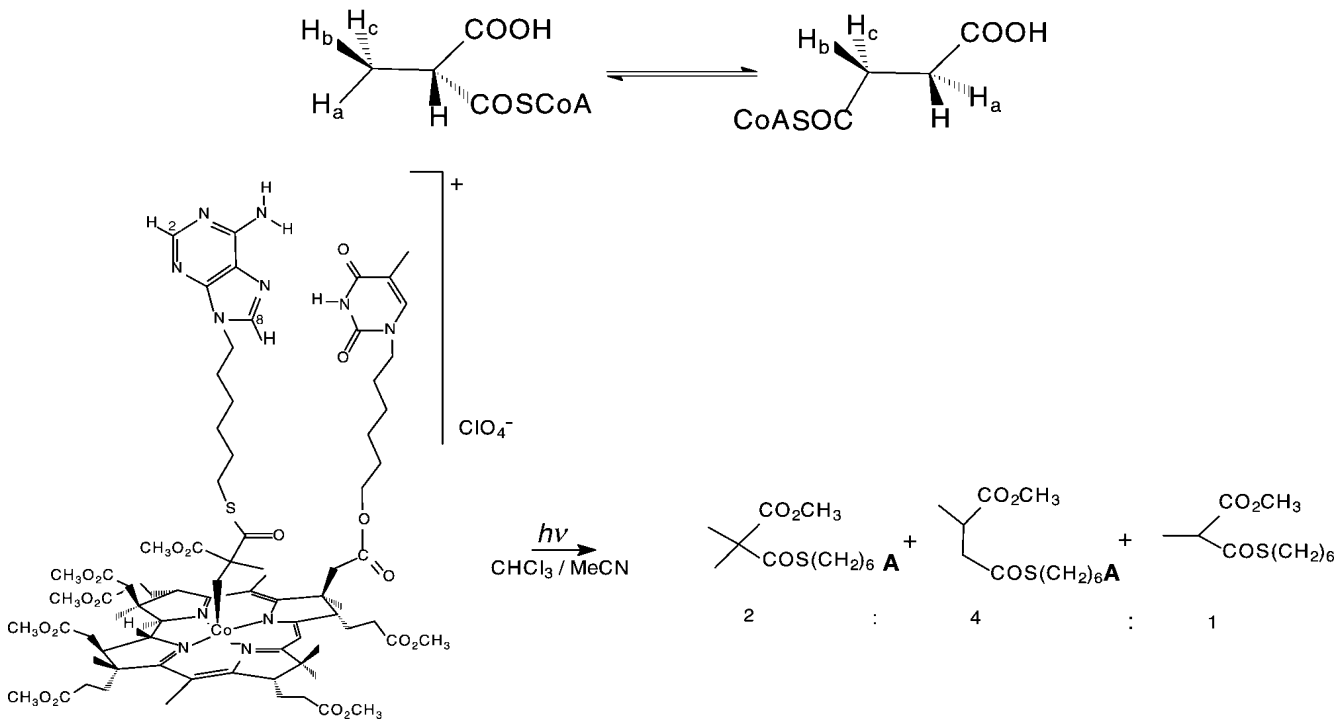
Models that introduce molecular recognition and binding of the vitamin-B_{12} derivatives and the corresponding substrates through hydrophobic interactions or H-bonds have been developed. Thus, these models have shown that such noncovalent interactions increase the degree of rearrangement by keeping the originally formed radical close to the Co corrinoid for a prolonged period of time [13–15].

We have already shown that adenine·thymine (A·T) base pairing is able to induce the rearrangement (*Scheme 1*), and we have now developed a new model incorporating the guanine·cytosine (G·C) base pair. Considering that the C·G association is hundred-fold stronger than A·T, the G·C interaction should favor the rearrangement more efficiently than A·T base pairing [16–19].

The syntheses of vitamin-B_{12}-derived complexes incorporating a cytosine and N^4-acetylcytosine moiety have already been reported [20]. Here we present the synthesis of the substrate containing a guanine moiety, namely the 2-(iodomethyl)-2-methyl-monothiomalonate **8**, the preparation of the corresponding alkylated vitamin-B_{12}-derived complexes, and the results of their irradiation.

Results and Discussion. – *Guanine Substrate* **8**. The guanine substrate **8** was prepared in five steps according to the sequence shown in *Scheme 2*. Direct N^9-alkylation of guanine does not provide a useful synthetic method due to the poor

Scheme 1. *The Methylmalonyl-Succinyl Rearrangement Catalyzed by the B_{12}-Dependent Methylmalonyl Mutase and the Model for the Methylmalonyl-Succinyl Rearrangement with Peripheral Adenine* (A) *and Thymine* (T) *Base Pairing*



solubility of guanine in organic solvents and the lack of regioselectivity between positions N(7) and N(9) [21–25]. Therefore, O^6-derivatives are normally used instead, even though regioselective alkylation is not always possible and a mixture of N^7- and N^9-alkylated compounds are formed. Our synthetic pathway required a guanine derivative that could provide selective N^9-alkylation and that could be deprotected, in the last step of the synthesis, under conditions compatible with the sensitive functional groups introduced within the N^9-substituent. A good solution was provided by O^6-[2-(trimethylsilyl)ethyl]guanine derivative **2**, which is regioselectively alkylated at N(9) and whose (trimethylsilyl)ethyl group can be easily removed [26] in the last step of the synthesis. Furthermore, the silyl group increases the solubility of the guanine derivatives in organic solvents, facilitating their isolation and characterization.

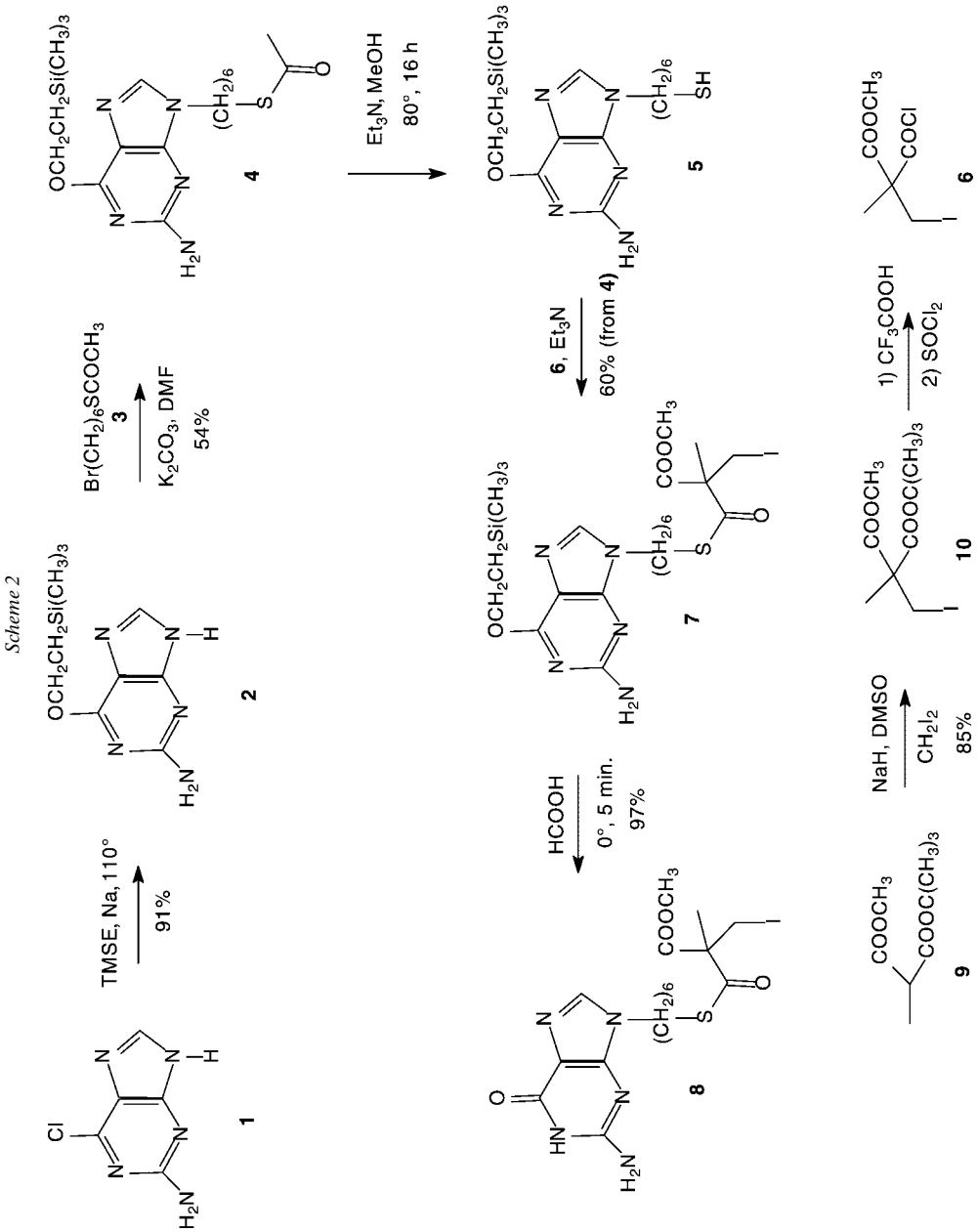
Thus, treatment of 6-chloropurinamine **1** with Na and 2-(trimethylsilyl)ethanol (TMSE) gave the O^6-substituted purinamine **2** in 91% yield (*Scheme 2*). Reaction of thioacetic acid *S*-(6-bromohexyl) ester (**3**) with **2** in the presence of K_2CO_3 afforded the N^2-alkylated compound **4** in 54% yield without the formation of the N^7-isomer. In contrast to the results described above, alkylation of 6-chloropurinamine **1** with **3** gave a mixture of the N^9- and N^7-substituted purinamines. Methanolysis of thioester **4** yielded quantitatively thiol **5**, which was used without further purification. Thiol **5** was added to methyl 2-(iodomethyl)-2-methylmalonic acid chloride **6** in the presence of Et_3N to yield **7** in good yield. The acid chloride **6** was prepared as follows: *tert*-butyl methyl 2-methylmalonate (**9**) was first treated with NaH and then with CH_2I_2 to give **10** (*Scheme 2*). Removal of the *tert*-butyl moiety with CF_3COOH and treatment with $SOCl_2$ gave the acid chloride **6**. The guanine substrate **8** was obtained in quantitative yield by treatment of the protected **7** with formic acid at 0° for 5 min followed by lyophilization.

Iodide **8** proved a suitable alkylating agent for the cytosine-containing vitamin-B_{12} derivatives as described below. The bromomethyl derivatives corresponding to **7** and **8** could also be prepared, in similar yields, following the same procedure with CH_2Br_2. However, the reaction of the vitamin-B_{12} derivative with the bromomethyl compounds afforded a mixture of products from which the alkylated complexes could not be separated.

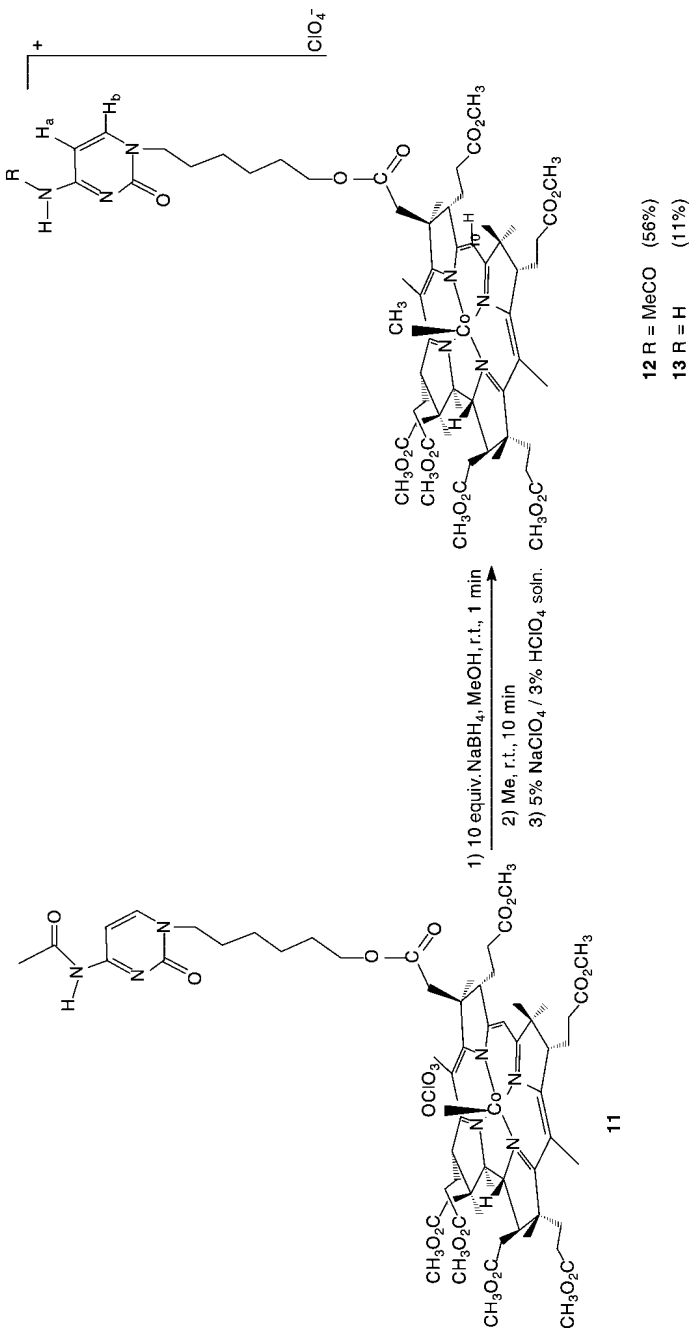
The synthesis of the highly functionalized guanine derivative **8** was achieved in few steps and in good yield.

G·C Complexes **16**–**18**. In the synthesis of vitamin-B_{12} derivatives incorporating a cytosine and an N^4-acetylcytosine moiety in the side chain of the corrin, reduction and deacetylation of the cytosine moiety in the presence of $NaBH_4$ were reported [20]. Therefore, before alkylating **11** with the guanine substrate **8**, the two-step alkylation procedure, namely, first reduction of Co^{II} to Co^{I} with $NaBH_4$, then treatment of the Co^{I} complex with the alkylating agent, was investigated with MeI. Thus, the vitamin-B_{12} derivative **11** was reduced with 10 mol-equiv. of $NaBH_4$ for 1 min to Co^{I} and then treated with excess MeI for 10 min to yield the methylated complex **12** and a second compound **13**, having the deacetylated cytosine moiety, in 56 and 11% yield, respectively (*Scheme 3*). In contrast to previous results, where methylation of cob(I)esters yielded β/α-coordination isomers, we obtained only the β-methylated compound **12**. When zinc was used for the reduction of **11**, the deacetylation took place to a larger extent, the products **12** and **13** being obtained in yields of 22 and 28%, respectively.

Scheme 2


TMSE, Na, 110°
91%
Br(CH2)6SCOCH3
3
K2CO3, DMF
54%
Et3N, MeOH
80°, 16 h
6, Et3N
60% (from 4)
HCOOH
0°, 5 min.
97%
NaH, DMSO
CH2I2
85%
1) CF3COOH
2) SOCl2

Scheme 3


1) 10 equiv. NaBH4, MeOH, r.t., 1 min
2) Me, r.t., 10 min
3) 5% NaClO4 / 3% HClO4 soln.
11
12 R = MeCO (56%)
13 R = H (11%)

The β-orientation of the Me ligand was determined by ^{1}H-NMR (*Fig. 1*): a signal at -0.11 ppm for **12** and at -0.10 ppm for **13** was observed for MeCo, *i.e.* chemical-shift values analogous to the ones observed for the Me–Co group in the β-methyl complexes with heptamethyl cobester [27] and a hexamethyl cobester containing a styrene side chain at the periphery [28]. For the α-isomers of the two latter complexes, the Me–Co signal appears at -0.21 as determined by NOE experiments. The ^{1}H-NMR spectrum and ESI-MS of **12** and **13** show for compound **12** the presence of the acetyl group (*Fig. 1*, at 2.23 ppm) and cytosine moiety, whereas a deacetylated cytosine moiety is present in **13**.

Due to the deacetylation, H_a of the cytosine group in **13** (see *Scheme 3*) is shifted upfield in comparison with **12**, the chemical-shift difference $\Delta\delta$ being *ca.* 1.16 ppm, whereas H_b is shifted only by 0.32 ppm[1]).

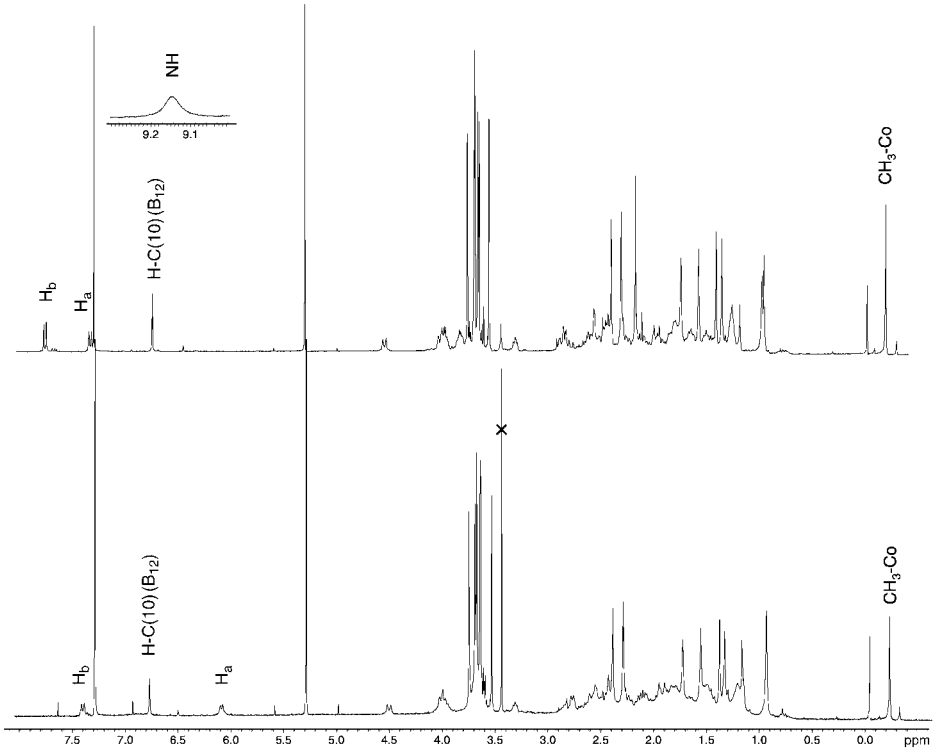


Fig. 1. *^{1}H-NMR* (300 MHz) *Spectra of* **12** (upper trace) *and* **13** (lower trace) *in* $CDCl_3$ (δ 5.3 CH_2Cl_2)

Reaction of substrate **8** with aquo-cyano-cobester **14** in the presence of $NaBH_4$ gave complex **15** as a *ca.* 1.5 : 1 mixture of two diastereoisomers in 15% yield (*Scheme 4*). The latter complex was identified by ^{1}H-NMR and ESI-MS and gave the data corresponding to the structure shown.

In spite of the propensity of the cytosine moiety in the vitamin-B_{12} derivatives to undergo deacetylation and reduction when treated with $NaBH_4$, it was possible to prepare and isolate by chromatography complex **16** (20% yield), after treatment of **11** with $NaBH_4$ (5 mol-equiv., 1 min) in MeOH and then with **8** (5 min); the concomitant formation of complex **17**, however, could not be avoided, and **17** was also isolated (6%)

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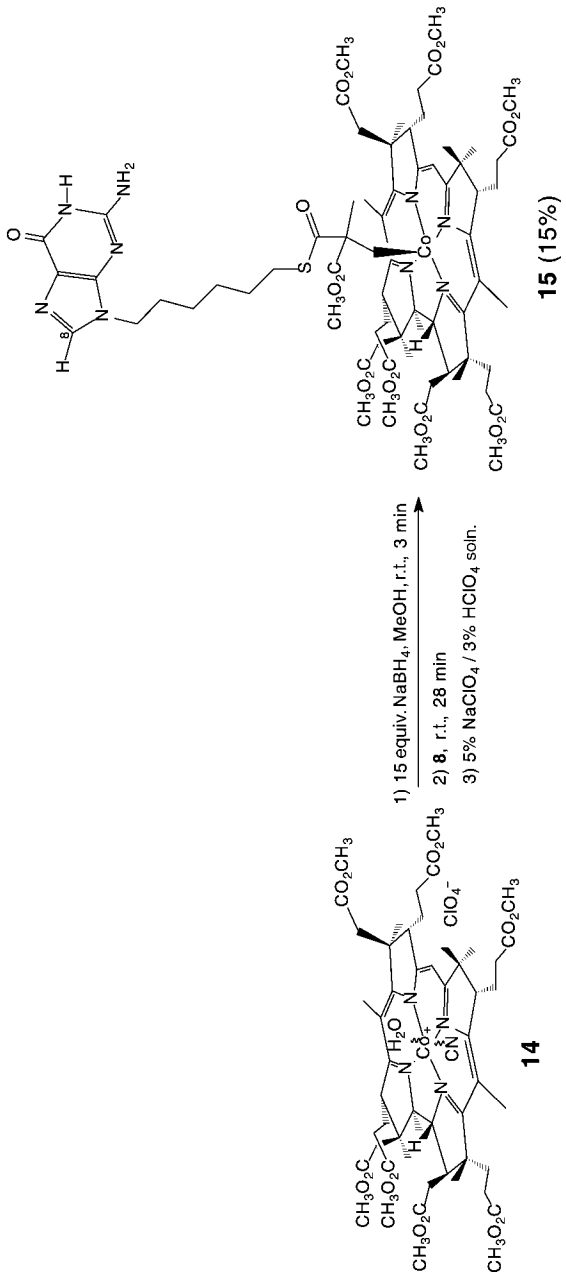
[1]) The differences in the ^{1}H-NMR chemical shifts for H–C(5) and H–C(6) of cytosine and N^4-acetylcytosine were determined for the vitamin-B_{12} derivatives [20] and for N^4-acetylcytidine and cytidine [29].

Scheme 4


1) 15 equiv. NaBH4, MeOH, r.t., 3 min
2) 8, r.t., 28 min
3) 5% NaClO4 / 3% HClO4 soln.
14
15 (15%)

and characterized (*Scheme 5*). Subsequently, the two diastereoisomers of **16** could be separated by column chromatography to give 7% **16a** and 12% **16b**.

When a large excess of $NaBH_4$ (*e.g.*, 58 mol-equiv) and a longer reaction time (3 min for reduction, 15 min for alkylation) were used, deacetylated **17** (18%) and reduced **18** (8%) were obtained, the latter being an isomer mixture due to the stereogenic C(4) of the reduced cytosine ring and the quaternary C-atom arising from **8**. The structure of **18** was confirmed by the isolation of the dicyano complex **21** after irradiation (see below), the latter having been previously prepared and fully characterized [20]. When **11** was reduced by zinc and then treated with **8**, complex **17** was formed in 18%, and the acetylated **16** could not be detected.

In the ^{1}H-NMR of the major isomer **16b** (*Fig. 2*), H_a and H_b of the acetylcytosine moiety appear at 7.40 and 7.84 ppm (7.34 and 7.74 ppm for **16a**), respectively; in the ^{1}H-NMR of the diastereomer mixture, all the peaks appear doubled, making a precise assignment difficult. The ESI-MS show a peak *m/z* 1652 ($[M - ClO_4]^+$) for **16** and at *m/z* 1610 ($[M - ClO_4]^+$) for **17** confirming their structures. The cytosine double-bond protons, H_a and H_b, are missing in the ^{1}H-NMR of **18**, and the ESI-MS shows a peak at *m/z* 1656 ($[M - ClO_4 - 1]^+$).

The ratio of acetylated/deaceatylated/reduced vitamin-B_{12}-derived complexes obtained depended on the reducing agent used to convert Co^{II} to Co^{I} and the reaction time. It was also observed that the fast deacetylation or reduction reaction of the cytosine moiety should be an intramolecular process since it occurs with **1** but does not

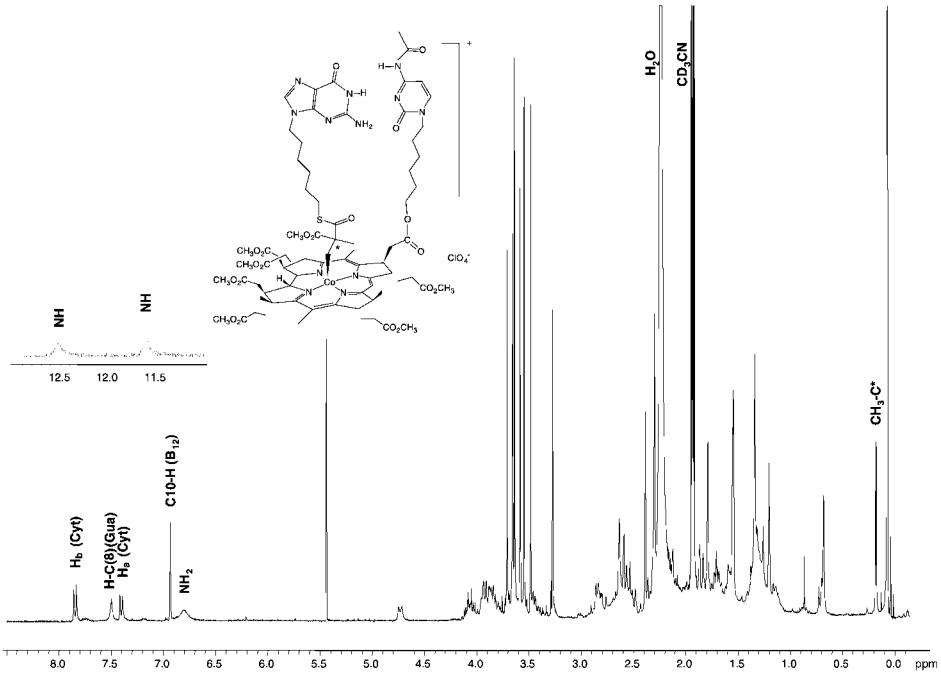
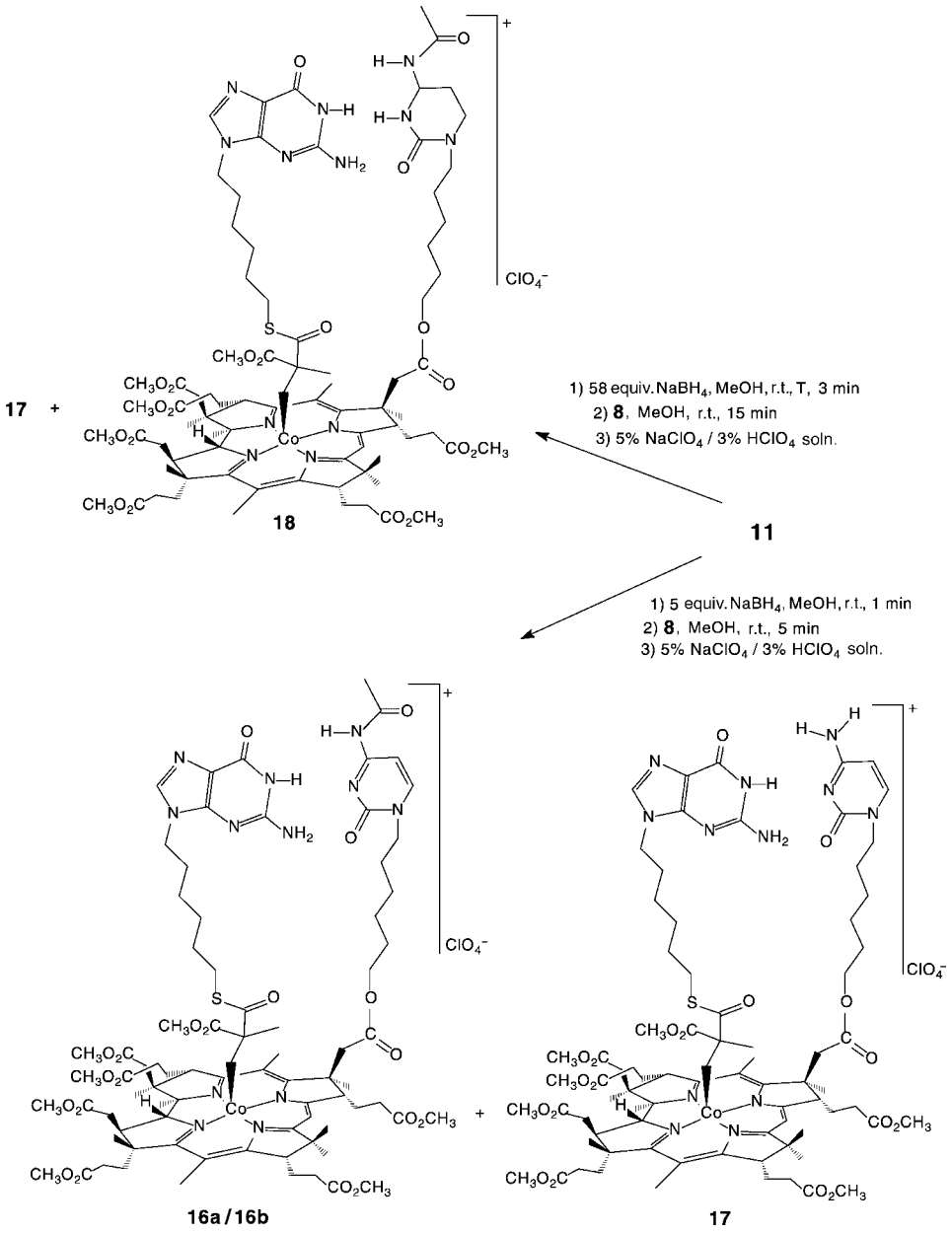


Fig. 2. *^{1}H-NMR* (300 MHz) *Spectrum of diastereoisomer* **16b** *in CD_3CN*

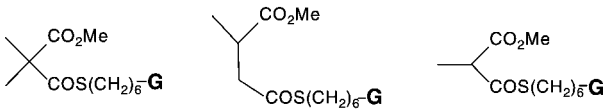
Scheme 5


17
18
1) 58 equiv. NaBH4, MeOH, r.t., T, 3 min
2) 8, MeOH, r.t., 15 min
3) 5% NaClO4 / 3% HClO4 soln.
11
1) 5 equiv. NaBH4, MeOH, r.t., 1 min
2) 8, MeOH, r.t., 5 min
3) 5% NaClO4 / 3% HClO4 soln.
16a/16b
17

occur when N^4-acetylcytosine and heptamethyl cob(II)ester were exposed to $NaBH_4$, under the reaction conditions and reaction time described above[2]).

Thus, due to the propensity of the cytosine side chain in vitamin-B_{12} derivatives to undergo reduction or deacetylation in the presence of $NaBH_4$, the preparation of the alkylated complexes with C·G moieties proved difficult. Preparation of complex **16** required a reactive iodomethyl derivative as the alkylating agent and fast conversion of Co^{II} to Co^{I} with $NaBH_4$. The nature of the cytosine moiety in the alkylated complexes **16**–**18** was confirmed by the isolation, after irradiation, of the known complexes **19**–**21** [20].

Irradiation. Compounds **16**–**18** were irradiated under Ar with a 150-W lamp in $CHCl_3$/MeCN 5 : 1, an aprotic noncompetitive solvent that should favor base pairing. To analyze the products, the irradiation mixture was separated into two fractions by column chromatography: the colored fractions containing the vitamin-B_{12}-derived complexes were treated further with 0.1M KCN to give the dicyano complexes **19**–**21** (*Scheme 6*). The colorless fractions were combined and separated by HPLC. Based on the previous results of the adenine·thymine model [14] (see *Scheme 1*), a mixture of three compounds, *e.g.*, **22** formed by H-abstraction of the radical generated by photolysis, the rearranged succinate **23**, and the fragmentation product **24**[3]) were expected (*Fig. 3*). Surprisingly, only the reduction compound **22** and the fragmentation compound **24** were found in the colorless fractions (*Scheme 6*), and no rearranged compound was observed. The irradiation experiment was repeated three times and proved to be reproducible with the amount of fragmentation product **24** varying slightly from one experiment to another.



22 **23** **24**

Fig. 3. *The three possible products* **22**–**24** *of the irradiation of vitamin-B_{12}-derived complexes*

Discussion. – The design of our model is based on two principles. First, on the solubility of the complexes in aprotic solvents that favor base pairing, and, second, on the flexibility of the C_6 alkyl chain connecting the corrin ring and the cytosine moiety, which is short enough to favor intramolecular pairing but at the same time provides enough flexibility for the guanine and the cytosine moieties to achieve the best conformation for H-bonding. Since the A·T interaction proved, previously, to induce rearrangement, it was surprising to find that thioester migration leading to succinate did not take place in the present model. We did not have, at that point, any evidence to explain the results. We could, however, observe that, due to the restrictions imposed by the C_6 alkyl chain, the *Hoogsteen* form could be favored in our model over the *Watson-*

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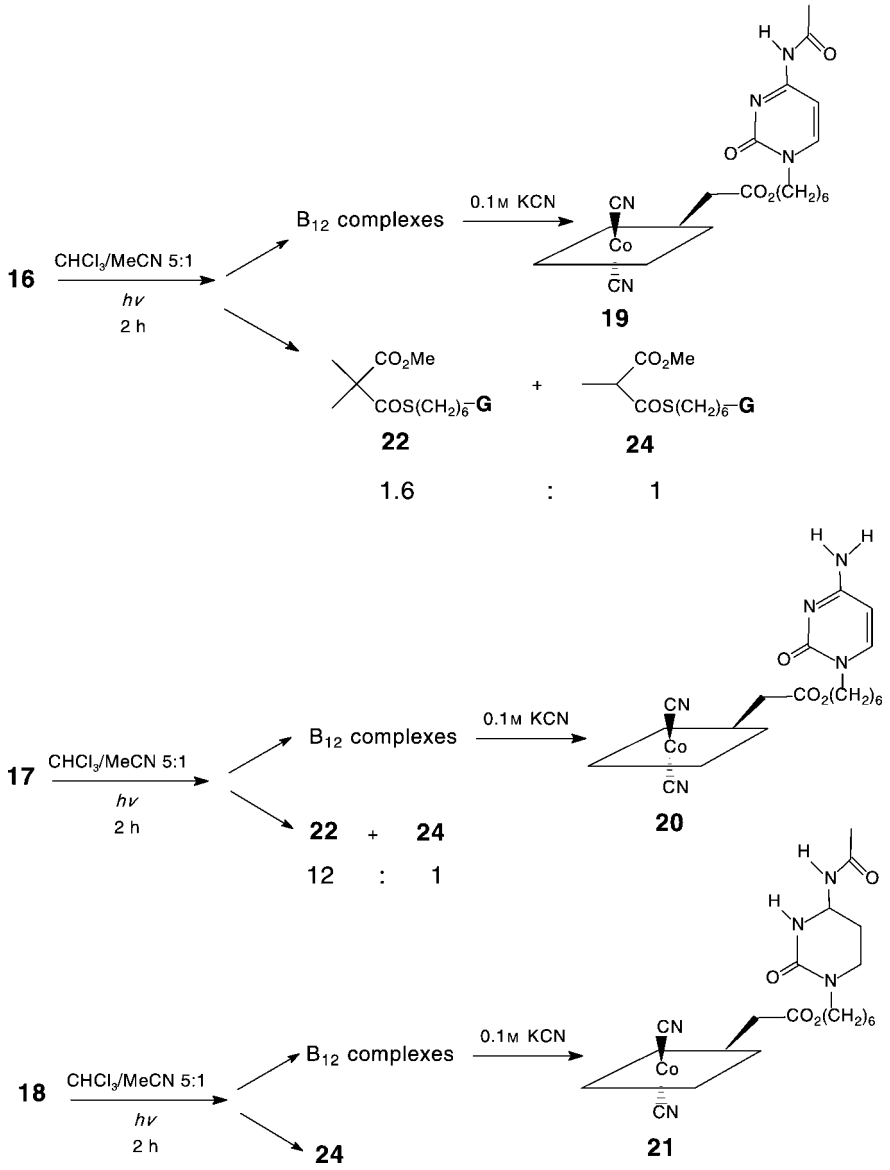
[2]) For another example of an intramolecular reaction of the side chain of vitamin-B_{12} derivatives bearing polyether groups, see [30].

[3]) The formation of methylmalonates has been shown previously to depend on the presence of O_2. For a discussion on the reaction conditions and the mechanistic implications, see [31].

Scheme 6. *Irradiation of the Complexes* **16** (acC·G), **17** (C·G), *and* **18** (ac(h)C·G) *and Isolation of the Vitamin-B_{12}-Dicyano Derivatives* **19**–**21**



Crick Base pair. The A·T base pairing can occur both *via Hoogsteen* or *Watson-Crick* interactions and both are of comparable energy. In the case of the G·C model, however, only the *Watson-Crick* interaction is possible (*Fig. 4*). An indication for the *Hoogsteen* interaction in the A·T model was obtained by ^{1}H-NMR·H–C(8) of adenine (8.01 ppm) in the A·T complex shown in *Scheme 1* is shifted by 0.20 ppm with

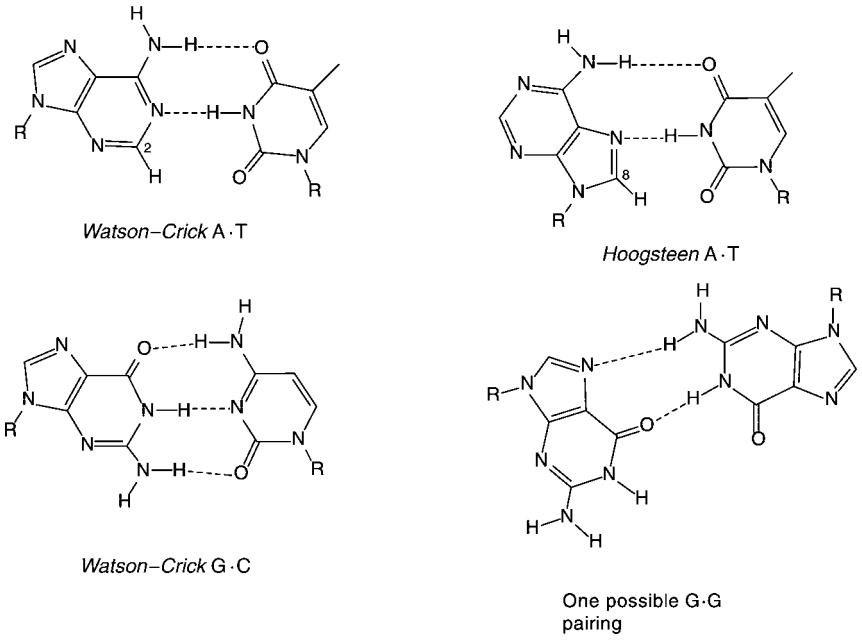


Fig. 4. *Possible H-bond interactions in adenine·thymine* (A·T), *guanine·cytosine* (C·G), *and guanine·guanine* (G·G)

respect to the H–C(8) (7.81 ppm) of the complex with heptamethyl cobester where the thymine moiety is absent, whereas H–C(2) of the adenine is shifted by 0.01 ppm in the same two complexes [32]. A significant downfield shift of H–C(8) implies the formation of the *Hoogsteen*-type H-bonds and a significant downfield shift of H–C(2) implies interaction of the *Watson-Crick* type. The H–C(8) (*Hoogsteen*) or H–C(2) (*Watson-Crick*) of adenine is deshielded by the thymine carbonyl group at C(2) as indicated in *Fig. 4* [33][34]. It was not possible to assign shifts of the exchangeable NH protons of complexes **15** and **16** to G·C interactions and, therefore, no conclusions could be reached regarding the bonding mode in the G·C complex. Although we have no evidence at the moment, it is possible that the attachment of the C_6 alkyl chain at N(9) places the atoms involved in H-bonds too far away so that the G·C binding does not take place, favoring intermolecular G·G interaction. The G·G interaction does not keep the alkyl radical formed by irradiation in the vicinity of the Co and, consequently, does not induce the rearrangement. As a result, in spite of the stronger binding of the G·C bases as compared to the A·T bases, only the latter induces rearrangement. However, further investigations of the structure of the complexes are necessary to explain the results obtained by irradiation of the new G·C complexes.

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Experimental Part

General. Reagents were purchased from *Fluka Chemie AG*. Sodium hydride: 55–65% dispersion. Solvents for chemical reactions and chromatography were distilled prior to use. DMF: *puriss.*, absolute, over molecular sieves ($H_2O \leq 0.01\%$); MeOH, CH_2Cl_2, and MeCN: *Romil*, super purity solvent; dry CH_2Cl_2: *puriss.*, absolute, over molecular sieves ($H_2O < 0.0005\%$). The synthesis, isolation, and detection of all alkylated complexes were done in the dark. Column chromatography (CC) and flash chromatography (FC): silica gel *60* (40–60 μm) from *Baker* (analyzed reagents); CC* and FC* indicate $NaClO_4$-impregnated silica gel [13]. Thin-layer chromatography (TLC): reactions monitored on *Alugram® Sil G/UV$_{254}$* from *Macherey-Nagel*, detection with a *Camag-53000* UV lamp (λ 254 nm) or an aq. $KMnO_4$ soln;. TLC* indicates that the sheets were soaked with 2% $NaClO_4$ (immerged in aq. 2% $NaClO_4$ soln. for a short time, dried in the air for 1 h, then dried at 110° for 2 h); R_f* is used correspondingly. Reversed-phase HPLC: *Jasco PU-980* pump; *Jasco UV-975* detector; *Lichrospher 60-RP-select-B* column (4 × 25 cm), *Merck*; stationary phase C_{18} (5 μm) UV/VIS: *Hewlett-Packard 8451-A* diode-array spectrophotometer; λ_{max} (log ε) in nm. IR: *Perkin-Elmer 1600 FTIR*; KBr discs or $CHCl_3$ soln. in 0.2-mm-path NaCl cells; in cm^{-1}. NMR: *Bruker AC-300* (^1H, 300 MHz; ^{13}C, 75 MHz) and *Bruker AC-500* (^1H, 500 MHz; ^{13}C, 125 MHz); δ in ppm rel. to $CDCl_3$ (δ(H) 7.27, δ(C) 77.00), CD_3OD (δ(H) 4.84, δ(C) 51.53), (D_6)DMSO (δ(H) 2.50 or CD_3CN (δ(H) 1.93, 2.30 (H_2O)), *J* in Hz; ^{13}C multiplicities from DEPT spectra. Mass spectra: EI: *Varian MAT-CH-7A*, 70 eV; LSI: *Fisions Instruments VG AutoSpec*, acceleration voltage 8 kV, ionization Cs^+ (32 keV), matrix 1,3-dithiothreitol (DTT)/1,3-dithioerythrol (DTE) 5:1; ESI: *Fisions Instrument VG Platform II*, positive-ion measurements (3.5 kV), solvent MeCN/H_2O 1:1; in *m*/*z* (%).

*6-[2-(Trimethylsilyl)ethoxy]-9*H*-purin-2-amine* (**2**). Na (0.18 g, 7.83 mmol) was dissolved in 2-(trimethylsilyl)ethanol (5 ml, 35.1 mmol) during 2 h at 110° under Ar, and after addition of 6-chloro-9*H*-purin-2-amine (500 mg, 2.95 mmol), the soln. was refluxed for 6 h. After cooling to r.t., AcOH (0.5 ml) was added, followed by hexane (35 ml). By centrifugation, the solid was separated from the liquid, and, after removal of the solvent, the unreacted 2-(trimethylsilyl)ethanol was recovered. The solid was dissolved in acetone (50 ml), and silica gel was added. After concentrating, the mixture obtained was submitted to FC (acetone/MeOH 100:0 → 90:10): 672.6 mg (91%) of **2**. White powder. R_f (AcOEt/MeOH/H_2O/AcOH 10:1:1:0.5) 0.59. ^1H-NMR (300 MHz, (D_6)DMSO): 0.09 (*s*, 9 H); 1.15 (*t*, *J* = 8.3, 2 H); 4.51 (*t*, *J* = 8.3, 2 H); 6.22 (*s*, 2 H); 7.81 (*s*, 1 H); 12.40 (*s*, 1 H).

Thioacetic Acid S-*(6-bromohexyl) Ester* (**3**). The mixture of potassium thioacetate (228.4 mg, 2.0 mmol) and 1,6-dibromohexane (1.464 g, 6.0 mmol) in EtOH (10 ml) was refluxed for 2 h. After removing the solvent, Et_2O was added, the org. soln. washed with H_2O (2×), dried ($MgSO_4$), and evaporated, and the product purified by CC (hexane/Et_2O 20:1): 359.6 mg (75%) of **3**. R_f (hexane/ether 20:1) 0.63. IR ($CHCl_3$): 3026*s*, 2329*m*, 2872*m*, 1703*s*, 1473*w*, 1439*w*, 1363*m*, 1267*m*, 1233*m*, 1147*m*, 1123*m*, 965*m*, 812*s*, 677*s*, 639*m*, 567*w*. ^1H-NMR (300 MHz, $CDCl_3$): 1.39 (*m*, 4 H); 1.56 (*m*, 2 H); 1.83 (*m*, 2 H); 2.30 (*s*, 3 H); 2.84 (*t*, *J* = 7.2, 2 H); 3.37 (*t*, *J* = 6.3, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 27.60 (*t*); 27.84 (*t*); 28.90 (*t*); 29.32 (*t*); 30.60 (*q*); 32.54 (*t*); 33.65 (*t*); 195.74 (*s*). MS: 240 (6, M^+), 238 (5, M^+), 197 (19), 180 (5), 159 (32), 141 (6), 117 (100), 99 (13), 83 (25), 55 (16), 43 (48). HR-MS: 238.0020 ($C_8H_{15}BrOS^+$; calc. 238.0027).

Thioacetic Acid S-*(6-{2-Amino-6-[2-(trimethylsilyl)ethoxy]-9*H*-purin-9-yl}hexyl) Ester* (**4**). The mixture of **2** (494.7 mg, 1.97 mmol), **3** (783.7 mg, 3.28 mmol), and K_2CO_3 (408.4 mg, 2.96 mmol) in DMF (8 ml) was stirred at r.t. overnight. After removing the DMF by distillation, the residue was submitted to CC (CH_2Cl_2/MeOH 30:1): 432.7 mg (54%) of **4**. R_f (CH_2Cl_2/MeOH 50:1) 0.54. IR ($CHCl_3$): 3668*w*, 3543*m*, 3419*s*, 3208*w*, 3035*s*, 2959*s*, 2863*m*, 2489*w*, 1684*s*, 1612*s*, 1521*s*, 1478*s*, 1463*s*, 1411*s*, 1363*s*, 1339*s*, 1286*m*, 1252*s*, 1190*m*, 1137*s*, 1075*s*, 1027*s*, 960*m*, 941*m*, 869*s*, 845*s*, 701*m*, 639*s*. ^1H-NMR (300 MHz, $CDCl_3$): 0.06 (*s*, 9 H); 1.20 (*t*, *J* = 8.5, 2 H); 1.25 (*m*, 4 H); 1.53 (*m*, 2 H); 1.81 (*m*, 2 H); 2.29 (*s*, 3 H); 2.81 (*t*, *J* = 7.2, 2 H); 4.01 (*t*, *J* = 7.2, 2 H); 4.55 (*t*, *J* = 8.6, 2 H); 4.93 (*s*, 2 H); 7.55 (*s*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): −1.41 (*q*); 17.55 (*t*); 26.03 (*t*); 28.07 (*t*); 28.86 (*t*); 29.29 (*t*); 29.65 (*t*); 30.60 (*q*); 43.30 (*t*); 64.80 (*t*); 115.69 (*s*); 139.08 (*d*); 153.81 (*s*); 159.31 (*s*); 161.39 (*s*); 195.85 (*s*). MS: 409 (44, M^+), 394 (12), 381 (36), 366 (26), 351 (5), 338 (100), 324 (27), 306 (51), 292 (54), 278 (31), 266 (16), 250 (10), 236 (51), 223 (21), 208 (67), 191 (7), 166 (8), 115 (30), 93 (15), 73 (35), 28 (26), 18 (50). HR-MS: 409.1953 ($C_{18}H_{31}N_5O_2SSi^+$; calc. 409.1968). Anal. calc. for $C_{18}H_{31}N_5O_2SSi$: C 52.78, H 7.63, N 17.10; found: C 52.54, H 7.80, N 16.84.

*6-{2-Amino-6-[2-(trimethylsilyl)ethoxy]-9*H*-purin-9-yl}hexane-1-thiol* (**5**). A soln. of **4** (182.3 mg, 0.45 mmol) in MeOH (40 ml) and Et_3N (20 drops) was refluxed for 16 h. After evaporation, crude **5** was obtained, which was used for the next step without purification. R_f (CH_2Cl_2/MeOH 40:1) 0.43. ^1H-NMR (300 MHz, $CDCl_3$): 0.03 (*s*, 9 H); 1.17 (*t*, *J* = 8.5, 2 H); 1.29 (*m*, 4 H); 1.52 (*m*, 2 H); 1.78 (*m*, 2 H); 2.45 (*m*, 2 H); 3.98 (*t*, *J* = 7.2, 2 H); 4.52 (*t*, *J* = 8.6, 2 H); 4.95 (*s*, 2 H); 7.53 (*s*, 1 H).

Methyl tert-*Butyl 2-(Iodomethyl)-2-methylmalonate* (**10**). Methyl *tert*-butyl 2-methylmalonate (**9**; 1.2784 g, 6.79 mmol) in abs. DMSO (2 ml) was added dropwise to the suspension of NaH (185.0 mg, 7.71 mmol) in abs. DMSO (6 ml). The resulting clear soln. was cooled to 14° and CH_2I_2 (3.46 g, 12.92 mmol) in abs. DMSO (2 ml) was added dropwise. After removing the cooling bath, the mixture was stirred 3.5 h at r.t., H_2O (40 ml) was added, and the mixture was extracted (3×) with hexane/Et_2O 10:1. The org. phase was washed with sat. NaCl soln. (2×), dried ($MgSO_4$), and evaporated. FC (hexane/Et_2O 4:1) gave 1.8961 g (85%) of **10**. R_f (hexane/Et_2O 4:1) 0.37. IR ($CHCl_3$): 3035*s*, 2987*s*, 2959*s*, 1736*s*, 1487*m*, 1473*s*, 1449*s*, 1406*m*, 1382*s*, 1377*s*, 1305*s*, 1262*s*, 1209*s*, 1161*s*, 1113*s*, 1061*m*, 998*m*, 955*w*, 912*m*, 859*s*, 582*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.40 (*s*, 9 H); 1.43 (*s*, 3 H); 3.49 (*s*, 2 H); 3.69 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 9.57 (*t*); 21.60 (*q*); 27.72 (*q*); 52.72 (*q*); 55.08 (*s*); 82.58 (*s*); 168.02 (*s*); 170.03 (*s*). MS: 328 (100, M^+), 313 (14), 297 (12), 272 (94), 255 (73), 241 (5), 227 (59), 201 (30), 145 (47), 101 (16), 57 (23). HR-MS: 328.0167 ($C_{10}H_{17}IO_4^+$; calc. 328.0172).

*Methyl 3-[(6-[2-Amino-6-[2-(trimethylsilyl)ethoxy]-9*H*-purin-9-yl]hexyl)thio]-2-(iodomethyl)-2-methylpropanoate* (**7**). A soln. of **10** (295.2 mg, 0.90 mmol) in CF_3COOH (2 ml) was stirred at r.t. for 1 h under Ar. After removal of the CF_3COOH, $SOCl_2$ (2 ml) was added, and the mixture was stirred at r.t. overnight. Excess $SOCl_2$ was removed by distillation. The obtained crude methyl 3-chloro-2-(iodomethyl)-2-methyl-3-oxopropanoate (**6**) was dissolved in dry CH_2Cl_2 (1.5 ml), and Et_3N (*puriss*, 0.15 ml) was added. The soln. was cooled in an ice bath, the above-prepared crude **5** in CH_2Cl_2 (7 ml) added dropwise, and the mixture then stirred at r.t. for 3 h. After evaporation, the residue was submitted directly to CC (AcOEt/hexane 1:1): 166.5 mg (60% from **4**) of **7**. R_f (CH_2Cl_2/MeOH 40:1) 0.40. IR ($CHCl_3$): 3553*m*, 3428*m*, 3026*s*, 2959*s*, 2863*m*, 1746*s*, 1679*s*, 1621*s*, 1597*s*, 1521*m*, 1463*s*, 1411*s*, 1387*m*, 1339*s*, 1291*m*, 1252*s*, 1176*m*, 1113*m*, 1080*s*, 1027*m*, 979*m*, 946*m*, 869*s*, 840*s*, 644*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.05 (*s*, 9 H); 1.19 (*t*, J = 8.6, 2 H); 1.32 (*m*, 4 H); 1.48–1.62 (*m*, superimposed 1.57 (*s*), 5 H); 1.80 (*m*, 2 H); 2.86 (*t*, J = 7.2, 2 H); 3.52 (*d*, J = 10.3, 1 H); 3.65 (*d*, J = 10.3, 1 H); 3.73 (*s*, 3 H); 4.00 (*t*, J = 7.2, 2 H); 4.54 (*t*, J = 8.5, 2 H); 4.91 (*s*, 2 H); 7.54 (*s*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): −1.38 (*q*); 9.41 (*t*); 17.54 (*t*); 22.16 (*q*); 25.97 (*t*); 28.02 (*t*); 28.89 (*t*); 29.18 (*t*); 29.63 (*t*); 43.25 (*t*); 53.20 (*q*); 61.27 (*s*); 64.79 (*t*); 115.70 (*s*); 139.06 (*d*); 153.82 (*s*); 159.29 (*s*); 161.38 (*s*); 169.41 (*s*); 196.15 (*s*). MS: 621 (4, M^+), 593 (3), 435 (10), 407 (7), 392 (6), 367 (10), 338 (45), 324 (7), 306 (25), 292 (19), 278 (11), 237 (11), 223 (7), 185 (28), 147 (9), 140 (9), 126 (39), 101 (30), 73 (84), 44 (100), 28 (18). LSI-MS (3-nitrobenzyl alcohol): 622 (100, $[M+1]^+$), 594 (24), 338 (15). HR-LSI-MS: 622.1380 ($C_{22}H_{37}IN_5O_4SSi^+$; calc. 622.1380). Anal. calc. for $C_{22}H_{36}IN_5O_4SSi$: C 42.51, H 5.84, N 11.27; found: C 42.66, H 6.21, N 11.12.

*Methyl 3-{[6-(2-Amino-1,6-dihydro-6-oxo-9*H*-purin-9-yl)hexyl]thio}-2-(iodomethyl)-2-methylpropanoate* (**8**). A soln. of **7** (69.4 mg, 0.112 mmol) in formic acid (98–100%, pure; 2 ml) was stirred at 0° for 5 min. The mixture was then quickly cooled (liq. N_2) for 10 min and lyophilized for 2 h: 56.5 mg (97%) of **8**. R_f (CH_2Cl_2/MeOH 10:1) 0.32. ^{1}H-NMR (300 MHz, CD_3OD): 1.25–1.43 (*m*, 4 H); 1.46–1.63 (*m*, superimposed 1.55 (*s*), 5 H); 1.71–1.88 (*m*, 2 H); 2.90 (*t*, J = 7.2, 2 H); 3.59 (*d*, J = 10.3, 1 H); 3.68 (*d*, J = 10.3, 1 H); 3.71 (*s*, 3 H); 4.03 (*t*, J = 7.2, 2 H); 7.69 (*s*, 1 H). ^{13}C-NMR (75 MHz, CD_3OD): 11.80 (*t*); 24.95 (*q*); 29.46 (*t*); 31.46 (*t*); 32.47 (*t*); 32.64 (*t*); 33.27 (*t*); 46.92 (*t*); 56.14 (*q*); 65.08 (*s*); 120.12 (*s*); 142.20 (*d*); 157.70 (*s*); 173.36 (*s*); 200.09 (*s*). MS: 521 (5, M^+), 506 (6), 350 (7), 336 (14), 302 (21), 289 (8), 275 (8), 246 (8), 233 (37), 219 (38), 204 (12), 190 (9), 178 (9), 165 (17), 151 (18), 128 (100), 116 (38), 101 (19), 87 (58), 67 (24), 60 (12), 55 (12), 41 (10), 28 (5). LSI-MS: 522 (100, $[M+1]^+$), 396 (20), 152 (13). HR-LSI-MS: 522.0688 ($C_{17}H_{25}IN_5O_4S^+$; calc. 522.0672). Anal. calc. for $C_{17}H_{24}IN_5O_4S$: C 39.16, H 4.64, N 13.43; found: C 38.67, H 4.69, N 13.22.

c-*{6-[4-(Acetylamino)-2-oxopyrimidin-1(2*H*)-yl]hexyl}* a,b,d,e,f,g-*Hexamethyl* Co*β*-*Methylcob(III)yrinate Perchlorate* (**12**) *and* c-*{6-[4-Amino-2-oxopyrimidin-1(2*H*)-yl]hexyl}* a,b,d,e,f,g-*Hexamethyl* Co*β*-*Methylcob(III)yrinate Perchlorate* (**13**).

Method 1: $NaBH_4$ Reduction. A soln. of **11** (19.6 mg, 0.0144 mmol) in MeOH (12 ml) was degassed in an ultrasound bath under Ar for 15 min and cooled to r.t. Upon addition of $NaBH_4$ (5.5 mg, 0.144 mmol) to the brown soln., the color changed immediately to green, and, after stirring for 1 min, MeI (0.3 ml, 4.81 mmol) was added (→ immediately orange). After stirring at r.t. for 10 min, the mixture was treated with 5% $NaClO_4$/3% $HClO_4$ soln. (5 ml, cooled to 0°). The mixture was extracted with CH_2Cl_2 and the org. phase dried through cotton and evaporated. The yellow products were isolated by CC* (CH_2Cl_2/MeOH 20:1): 11.0 mg (56%) of **12** and 2.1 mg (11%) of **13**.

Data of **12**: R_f* (CH_2Cl_2/MeOH 20:1) 0.45. ^{1}H-NMR (300 MHz, $CDCl_3$): −0.11 (*s*, 3 H); 0.95–3.00 (*m*, superimposed 1.03 (*s*), 1.05 (*s*), 1.25 (*s*), 1.33 (*s*), 1.42 (*s*), 1.47 (*s*), 1.63 (*s*), 1.80 (*s*), 2.23 (*s*), 2.36 (*s*), 2.45 (*s*), total 59 H); 3.34 (*m*, 1 H); 3.55–4.13 (*m*, superimposed 3.59 (*s*), 3.68 (*s*), 3.69 (*s*), 3.72 (*s*), 3.73 (*s*), 3.79 (*s*), total 23 H); 4.56 (*d*, J = 9.5, 1 H); 6.72 (*s*, 1 H); 7.30 (*d*, J = 7.0, 1 H); 7.72 (*d*, J = 7.0, 1 H); 9.14 (*s*, 1 H). ESI-MS: 1273 (40, $[M-ClO_4]^+$), 648 (49), 637 (100, $[M-ClO_4]^{2+}$), 630 (45, $[M-ClO_4-Me]^{2+}$).

Data of **13**: R_f* (CH_2Cl_2/MeOH 20:1) 0.33. ^{1}H-NMR (300 MHz, $CDCl_3$): −0.10 (*s*, 3 H); 0.75–3.00 (*m*, superimposed 1.04 (*s*), 1.26 (*s*), 1.42 (*s*), 1.48 (*s*), 1.64 (*s*), 1.81 (*s*), 2.37 (*s*), 2.46 (*s*), total 56 H); 3.36 (*m*, 1 H); 3.50–4.15 (*m*, superimposed 3.59 (*s*), 3.69 (*s*), 3.70 (*s*), 3.72 (*s*), 3.75 (*s*), 3.80 (*s*), total 23 H); 4.55 (*d*, *J* = 10.3, 1 H); 6.14 (*d*, *J* = 7.7, 1 H); 6.73 (*s*, 1 H); 7.40 (*d*, *J* = 7.7, 1 H). ESI-MS: 1231 (5, $[M - ClO_4]^+$), 821 (8), 622 (21), 616 (100, $[M - ClO_4]^{2+}$), 609 (80, $[M - ClO_4 - Me - 1]^{2+}$).

Method 2: Zn Reduction. A soln. of **11** (15.0 mg, 0.011 mmol) in MeOH (10 ml) was degassed in an ultrasound bath under Ar for 15 min and cooled to r.t. After addition of NH_4Cl (20 mg) and active Zn powder (100 mg) to the brown soln., the color changed gradually to green. After 10 min, Me (0.3 ml, 4.81 mmol) was added (→ immediately orange). After stirring at r.t. for 1 min, the mixture was treated with 5% $NaClO_4$/3% $HClO_4$ soln. (5 ml, cooled to 0°) and worked up as above. The yellow products were separated by CC* (CH_2Cl_2/MeOH 18:1): 3.4 mg (22%) of **12** and 4.1 mg (28%) of **13**.

a,b,c,d,e,f,g-*Heptamethyl* Co*β-((2*R- *and 2*S*)-3-{[6-(2-Amino-1,6-dihydro-6-oxo-9*H*-purin-9-yl)hexyl]thio}-2-(methoxycarbonyl)-2-methyl-3-oxopropyl)cob(III)yrinate Perchlorate* (**15**). To a degassed soln. of **14** (20.6 mg, 0.0174 mmol) in MeOH (10 ml) under Ar was added $NaBH_4$ (10.0 mg, 0.264 mmol). The color changed immediately from brown to green, and, after stirring for 3 min, **8** (21.2 mg, 0.0447 mmol) in MeOH (4 ml, degassed as above) was added in the dark (→ orange). After stirring at r.t. for 28 min, the mixture was treated with 5% $NaClO_4$/3% $HClO_4$ soln. (4 ml, cooled to 0°) and worked up as above. CC (*Sephadex LH-20*, MeOH) and then CC* (CH_2Cl_2/MeOH 100:6) gave 4.0 mg (15%) of yellow **15**. R_f* (CH_2Cl_2/MeOH 10:1) 0.53. ^{1}H-NMR (300 MHz, CD_3OD): −0.19 (*s*, 1.8 H); 0.12 (*s*, 1.2 H); 0.40 (*d*, *J* = 6.6, 0.6 H); 0.50–3.00 (*m*, superimposed 0.59 (*s*), 1.10 (*s*), 1.14 (*s*), 1.25 (*s*), 1.42 (*s*), 1.47 (*s*), 1.50 (*s*), 1.67 (*s*)); 3.25–3.97 (*m*, superimposed 3.26 (*s*), 3.35 (*s*), 3.40 (*s*), 3.46 (*s*), 3.52 (*s*), 3.53 (*s*), 3.56 (*s*), 3.60 (*s*)); 6.93, 6.96 (2*s*, total 1 H); 7.50 (*s*, 1 H). ESI-MS: 1431 (27, $[M - ClO_4]^+$), 1037 (73, $[M - ClO_4 - Gua(CH_2)_6SCOC(Me)(COOMe)CH_2]^{2+}$), 519 (100, $[M - ClO_4 - Gua(CH_2)_6SCOC(Me)(COOMe)CH_2]^{2+}$), 482 (24).

c-*[6-[4-(Acetylamino)-2-oxopyrimidin-1(2*H*)-yl]hexyl]* a,b,d,e,f,g-*Hexamethyl* Co*β-((2*R*)- and (2*S*)-3-{[6-(2-Amino-1,6-dihydro-6-oxo-9*H*-purin-9-yl)hexyl]thio}-2-(methoxycarbonyl)-2-methyl-3-oxopropyl)cob(III)yrinate Perchlorate* (**16**) *and* c-*[6-[4-Amino-2-oxopyrimidin-1(2*H*)-yl]hexyl]* a,b,d,e,f,g-*Hexamethyl* Co*β-{(2*R*)- and (2*S*)-3-{[6-(2-Amino-1,6-dihydro-6-oxo-9*H*-purin-9-yl)hexyl]thio}-2-(methoxycarbonyl)-2-methyl-3-oxopropyl)cob(III)yrinate Perchlorate* (**17**). To a degassed soln. of **11** (52.0 mg, 0.038 mmol) in MeOH (8 ml) under Ar at r.t. was added $NaBH_4$ (7.2 mg, 0.190 mmol). The color changed immediately from brown to green. After stirring for 1 min, the degassed soln. of **8** (59.4 mg, 0.114 mmol) in MeOH (3 ml) was added (→ orange). After stirring at r.t. for 5 min, the mixture was treated with 5% $NaClO_4$/3% $HClO_4$ soln. (5 ml, cooled to 0°) and worked up as above. CC (*Sephadex LH-20*, MeOH, twice) and then CC* (CH_2Cl_2/MeOH 18:1) yielded 4.6 mg (7%) of **16a**, 8.0 mg (12%) of **16b** and 4.1 mg (6.3%) of **17** (mixture of diastereoisomers). UV/VIS of **16a**/**16b** ($5 \cdot 10^{-5}$M in $CHCl_3$/MeCN 5:1): 268 (4.30), 296 (4.53), 424 (4.15), 488 (4.06).

Data of **16a**: R_f* (CH_2Cl_2/MeOH 15:1) 0.33. ^{1}H-NMR (300 MHz, CD_3CN): 0.18 (*s*, 3 H); 0.60–3.00 (*m*, superimposed 1.20 (*s*), 1.34 (*s*), 1.54 (*s*), 1.79 (*s*), 1.93 (*m*, CD_3CN), 2.24 (*s*, CD_3CN), 2.30 (*s*), 2.39 (*s*)); 3.15–4.18 (*m*, superimposed 3.27 (*s*), 3.48 (*s*), 3.55 (*s*), 3.59 (*s*), 3.64 (*s*), 3.66 (*s*), 3.71 (*s*)); 4.73 (*d*, *J* = 9.9, 1 H); 6.80 (br. *s*, 2 H); 6.93 (*s*, 1 H); 7.40 (*d*, *J* = 7.4, 1 H); 7.50 (*s*, 1 H); 7.84 (*d*, *J* = 7.4, 1 H); 11.61 (br. *s*, 1 H); 12.52 (br. *s*, 1 H). ESI-MS: 1652 (1, $[M - ClO_4 - 1]^+$), 1258 (6, $[M - ClO_4 - Gua(CH_2)_6SCOC(Me)(COOMe)CH_2]^+$), 629 (100, $[M - ClO_4 - Gua(CH_2)_6SCOC(Me)(COOMe)CH_2]^{2+}$).

Data of **16b**: R_f* (CH_2Cl_2/MeOH 15:1) 0.31. ^{1}H-NMR (300 MHz, CD_3CN): −0.11 (*s*, 3 H); 0.48 (*d*, *J* = 6.6, 1 H); 0.60–3.00 (*m*, superimposed 1.23 (*s*), 1.26 (*s*), 1.35 (*s*), 1.59 (*s*), 1.78 (*s*), 1.93 (*m*, CD_3CN), 2.24 (*s*, CD_3CN), 2.43 (*s*)); 3.15–4.18 (*m*, superimposed 3.34 (*s*), 3.50 (*s*), 3.54 (*s*), 3.58 (*s*), 3.64 (*s*), 3.67 (*s*), 3.71 (*s*)); 4.68 (*d*, *J* = 9.9, 1 H); 6.97 (br. *s*, 3 H); 7.34 (*d*, *J* = 7.0, 1 H); 7.52 (*s*, 1 H); 7.81 (*d*, *J* = 7.0, 1 H); 11.25 (br. *s*, 1 H); 12.36 (br. *s*, 1 H). ESI-MS: 1652 (1, $[M - ClO_4 - 1]^+$), 1258 (6, $[M - ClO_4 - Gua(CH_2)_6SCOC(Me)(COOMe)CH_2]^+$), 629 (100, $[M - ClO_4 - Gua(CH_2)_6SCOC(Me)(COOMe)CH_2]^{2+}$).

Data of **17**: R_f* (CH_2Cl_2/MeOH 15:1) 0.23. ^{1}H-NMR (300 MHz, CD_3CN): −0.23 (*s*); −0.08 (*s*); 0.14 (*d*); 1.0–2.9 (several *m* overlapped with *s* and MeCN); 3.15 (*s*); 3.25 (*s*); 3.3–3.6 (8*s*); 3.82 (*m*); 4.53 (*d*); 5.68 (*d*); 6.25 (br. *s*); 6.79 (*d*); 7.17 (*s*); 7.35 (*m*); 11.29 (br. *s*). ESI-MS: 1610 (3, $[M - ClO_4 - 1]^+$), 1216 (18, $[M - ClO_4 - Gua(CH_2)_6SCOC(Me)(COOMe)CH_2]^+$), 817 (19), 806 (91, $[M - ClO_4]^{2+}$), 742 (47), 622 (14), 608 (100, $[M - ClO_4 - Gua(CH_2)_6SCOC(Me)(COOMe)CH_2]^{2+}$), 544 (69), 522 (32).

Cob(III)yrinate Perchlorate **17** *and* c-*[6-[4-(Acetylamino)-3,4,5,6-tetrahydro-2-oxopyrimidin-1(2*H*)-yl]hexyl]* a,b,d,e,f,g- *and Hexamethyl* Co*β-((2*R*)- and (2*S*)-3-{[6-(2-Amino-1,6-dihydro-6-oxo-9*H*-purin-9-yl)hexyl]thio} 2-(methoxycarbonyl)-2-methyl-3-oxopropyl)cob(III)yrinate Perchlorate* (**18**). To a soln. of **11** (36.9 mg, 0.0272 mmol) in degassed MeOH (12 ml), $NaBH_4$ (59.6 mg, 1.58 mmol) was added. The color changed immediately from brown to green. After stirring for 3 min, the degassed soln. of **8** (42.5 mg, 0.0816 mmol) in

MeOH (4 ml) was added (→ orange). After stirring at r.t. for 15 min, the mixture was treated with 5% $NaClO_4$/3% $HClO_4$ soln. (15 ml, cooled to 0°) and worked up as above. CC (*Sephadex LH-20*, MeOH, twice) and then CC* (CH_2Cl_2/MeOH 10:1) gave 8.4 mg (18%) of **17** and 4.1 mg (8.6%) of **18**.

Data of **17**: R_f* (CH_2Cl_2/MeOH 10:1) 0.37.

Data of **18**: R_f* (CH_2Cl_2/MeOH 10:1) 0.25. ^{1}H-NMR (300 MHz, CD_3CN): –0.34, 0.05 (2*s*, together 3 H); 0.28 (*d*, 2 H); 0.43 (*s*, 3 H); 0.58 (*m*, 2 H); 0.7–1.4 (*m*, overlapped with 0.99 (*s*), 1.09 (*s*), 1.11 (*s*), 1.22 (*s*), 1.33 (*s*)); 1.4–2.7 (*m*, overlapped with 1.52 (*s*), 2.04 (*s*), 2.15 (*s*), 2.18 (*s*)); 2.85–3.05 (*m*, overlapped with 2.96 (*s*), 3.00 (*s*)); 3.11 (*s*); 3.23 (*s*); 3.29 (*s*); 3.32 (*s*); 3.39 (*s*); 3.44 (*s*); 3.46 (*s*); 3.68 (*s*); 3.70 (*s*); 3.73 (*s*); 3.55–3.8 (*m*, 6 H); 4.41–4.50 (2*d*, 1 H); 4.83 (br. *s*, 1 H); 5.6 (br. *s*, 2 H); 6.26 (2br. *s*, 1 H); 6.70, 6.72 (2*s*, together 2 H); 7.46 (*s*, overlapped with a br. *s*, together 2 H). ESI-MS: 1656 (4, $[M-ClO_4-1]^+$), 1262 (65, $[M-ClO_4-Gua(CH_2)_6SCOC(Me)(COOMe)CH_2]^+$), 898 (13), 840 (76), 760 (31), 631 (61, $[M-ClO_4-Gua(CH_2)_6SCOC(Me)(COOMe)CH_2]^{2+}$), 602 (100), 565 (13), 523 (80).

Zn Reduction to **17**. To a degassed soln. of **8** (20.4 mg, 0.015 mmol) in MeOH (8 ml) were added NH_4Cl (20 mg) and active Zn powder (100 mg). The color changed slowly from brown to green. After 30 min, **8** (23.4 mg, 0.045 mmol) in degassed MeOH (2.5 ml) was added in the dark (→ quickly orange). After stirring at r.t. for 5 min, the mixture was treated with phosphate buffer pH 6 containing 1% $NaClO_4$ (5 ml) and worked up as above. CC (*Sephadex LH-20*, MeOH, twice) and then CC* (CH_2Cl_2/MeOH 15:1) gave 1.5 mg (6%) of **17a** (R_f* (CH_2Cl_2/MeOH 18:1) 0.31) and 3.1 mg (12%) of **17b** (R_f* (CH_2Cl_2/MeOH 18:1) 0.28), both isomers as yellow solid.

Photolysis of Complex **16**. Complex **16** (9.0 mg, 0.0051 mmol) was dissolved in $CHCl_3$ (10 ml; 'reinst', *Siegfried Handel AG*; filtered through basic Al_2O_3, degassed under Ar for 20 min and cooled to r.t.) and MeCN (2 ml; HPLC-grade, degassed under Ar for 20 min and cooled to r.t.) in the dark. After degassing under Ar for 15 min, the O_2-free soln. was irradiated by a 150-W lamp from a distance of 40 cm for 2 h while cooling with a fan. The soln. was concentrated and submitted to FC* (CH_2Cl_2/MeOH 18:1 → 10:1). The colored fraction (vitamin-B_{12}-derived complexes) was evaporated, the residue dissolved in CH_2Cl_2, then 0.1M KCN was added and the mixture treated in ultrasound bath for 15 min and extracted with CH_2Cl_2: compound **19**. The remaining fractions were combined (22.3 mg), separated, and analyzed by HPLC: **22**/**24** 1.6:1 (peak areas).

Photolysis of Complex **17**. Same procedure as above, with **17** (8.6 mg, 0.0050 mmol), $CHCl_3$ (10 ml), MeCN (2 ml). FC* (CH_2Cl_2/MeOH 15:1 → 10:1) gave **20** from the colored fraction. The remaining fractions were combined (18.1 mg), separated, and analyzed by HPLC: **22**/**24** 12:1 (peak areas).

Photolysis Complex **18**. Same procedure as above, with **18** (4.1 mg, 0.0023 mmol), $CHCl_3$ (8 ml), and MeCN (1.5 ml). FC* (CH_2Cl_2/MeOH 15.1 → 10:1) gave **21** from the colored fraction. The remaining fractions were combined (20.7 mg), separated, and analyzed by HPLC: only **24**.

*Methyl 3-[[6-(2-Amino-1,6-dihydro-6-oxo-9*H*-purin-9-yl)hexyl]thio}-2,2-dimethyl-3-oxopropanoate* (**22**). Isolated by HPLC. R_f (CH_2Cl_2/MeOH 10:1) 0.31. ^{1}H-NMR (300 MHz, 3.5 ml $CDCl_3$ + 1.0 ml CD_3OD, rel. to 7.27): 1.09–1.27 (*m*, 4 H); 1.30 (*s*, 6 H); 1.35–1.47 (*m*, 2 H); 1.58–1.72 (*m*, 2 H); 2.70 (*t*, *J* = 7.2, 2 H); 3.55 (*s*, 3 H); 3.82 (*t*, *J* = 7.2, 2 H); 7.39 (*s*, 1 H). ^{13}C-NMR (75 MHz, 3.5 ml $CDCl_3$ + 1.0 ml CD_3OD, rel. to 77.00): 22.75 (*q*); 25.74 (*t*); 27.86 (*t*); 28.52 (*t*); 28.81 (*t*); 29.54 (*t*); 43.29 (*t*); 52.43 (*q*); 56.90 (*s*); 116.60 (*s*); 137.74 (*d*); 151.21 (*s*); 153.23 (*s*); 158.03 (*s*); 173.12 (*s*); 200.54 (*s*). MS: 396 (8, $[M+1]^+$), 377 (23), 338 (68), 305 (45), 291 (18), 281 (41), 267 (22), 248 (44), 234 (51), 220 (36), 206 (24), 192 (22), 178 (27), 165 (38), 151 (27), 44 (100), 31 (20). LSI-MS: 791 (7, $[2M+1]^+$), 396 (100, $[M+1]^+$). HR-LSI-MS: 396.1708 ($C_{17}H_{26}N_5O_4S^+$; calc. 396.1706). Anal. calc. for $C_{17}H_{25}N_5O_4S$: C 51.63, H 6.37, N 17.71; found: C 51.46, H 6.49, N 17.60.

*Methyl 3-[[6-(2-Amino-1,6-dihydro-6-oxo-9*H*-purin-9-yl)hexyl]thio}-2-methyl-3-oxopropanoate* (**24**). R_f (CH_2Cl_2/MeOH 10:1) 0.31. ^{1}H-NMR (300 MHz, 3.5 ml $CDCl_3$ + 1.0 ml CD_3OD, rel. to 7.27): 1.14–1.35 (*m*, superimposed 1.28 (*d*, *J* = 7.4, 7 H); 1.39–1.54 (*m*, 2 H); 1.63–1.76 (*m*, 2 H); 2.76 (*t*, *J* = 7.2, 2 H); 3.53 (*q*, *J* = 7.2, 1 H); 3.59 (*s*, 3 H); 3.89 (*t*, *J* = 7.2, 2 H); 7.54 (*s*, 1 H).

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