6-(Diazomethyl)-1,3-bis(methoxymethyl)uracil, Synthesis and Transformation into Annulated Pyrimidinediones

by **Fuyi Zhang**, **Anna Kulesza**, **Shikha Rani**, **Bruno Bernet**, and **Andrea Vasella***

Laboratory of Organic Chemistry, Department of Chemistry and Applied Biosciences, ETH Zurich, Wolfgang Pauli-Strasse 10, CH-8093 Zurich
(e-mail: vasella@org.chem.ethz.ch)

6-(Diazomethyl)-1,3-bis(methoxymethyl)uracil (**5**) was prepared from the known aldehyde **3** by hydrazone formation and oxidation. Thermolysis of **5** and deprotection gave the pyrazolo[4,3-*d*]pyrimidine-5,7-diones **7a** and **7b**. $Rh_2(OAc)_4$ catalyzed the transformation of **5** into to a 2:1 (*Z*)/(*E*) mixture of 1,2-diuracilylethenes **9** (67%). Heating (*Z*)-**9** in 12N HCl at 95° led to electrocyclisation, oxidation, and deprotection to afford 73% of the pyrimido[5,4-*f*]quinazolinetetraone **12**. The $Rh_2(OAc)_4$-catalyzed reaction of **5** with 3,4-dihydro-2*H*-pyran and 2,3-dihydrofuran gave *endo*/*exo*-mixtures of the 2-oxabicyclo[4.1.0]heptane **13** (78%) and the 2-oxabicyclo[3.1.0]hexane **15** (86%), Their treatment with $AlCl_3$ or Me_2AlCl promoted a vinylcyclopropane–cyclopentene rearrangement, leading to the pyrano- and furanocyclopenta[1,2-*d*]pyrimidinediones **14** (88%) and **16** (51%), respectively. Similarly, the addition product of **5** to 2-methoxypropene was transformed into the 5-methylcyclopenta-pyrimidinedione **18** (55%). The $Rh_2(OAc)_4$-catalyzed reaction of **5** with thiophene gave the *exo*-configured 2-thiabicyclo[3.1.0]hexane **19** (69%). The analoguous reaction with furan led to 8-oxabicyclo[3.2.1]oct-2-ene **20** (73%), and the reaction with (*E*)-2-styrylfuran yielded a diastereoisomeric mixture of hepta-1,4,6-trien-3-ones **21** (75%) that was transformed into the (1*E*,4*E*,6*E*)-configured hepta-1,4,6-trien-3-one **21** (60%) at ambient temperature.

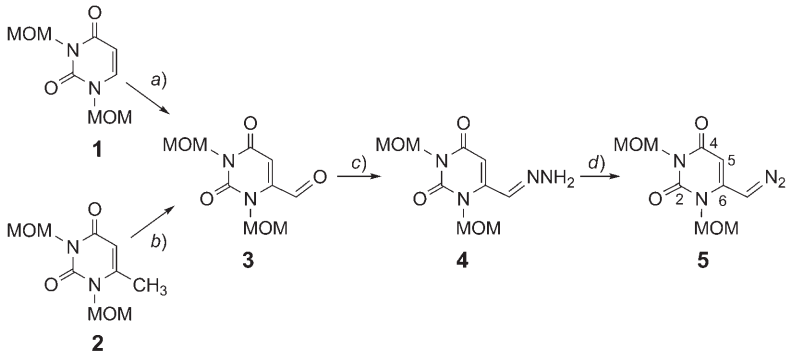
Introduction. – 6-Formyluridines are intermediates in the synthesis of novel oligoribonucleotide analogues ('ONIBs'; see [1][2] and refs. cit. there). Diazo compounds derived from 6-formyluracils, however, have (to the best of our knowledge) not been reported, perhaps surprisingly, considering the large number of pyrimidine syntheses and the broad interest in 5,6-disubstituted and 6-monosubstituted pyrimidine derivatives[1]) [4–6], and in uridine, uracil, and their derivatives and analogues [7–10]. The closest analogues of the envisioned vinylogous α-diazocarbonyl compounds derived from 6-formyluracils are 6-substituted sulfoxonium ylides. *Norris* and *Shechter* synthesized such ylides by treating 6-chloro-1,3-dimethyluracil with dimethylsulfoxonium methylide [11] and used them for the synthesis of 6-cyclopropyluracils, 5,6-methyleneuracils, and indirectly of uracils fused to seven-membered rings. Considering the versatility of diazo compounds and particularly of stable α-diazocarbonyl compounds [12–15], and more specifically their use for the synthesis of cyclopropanes [16], for X–H insertions (X = C, N, O, or S) [17][18], and as 1,3-dipoles [19], we considered it worthwhile to synthesize at least one such diazo compound, characterize

[1]) Many 6-substituted uracils were synthesized from 6-chloro-1,3-dimethyluracil *via* nucleophilic displacement [3].

it, and explore some of its transformations into known and new heterocyclic systems. Our choice fell on the *N*-protected 6-(diazomethyl)uracil **5** (*Scheme 1*).

Results and Discussion. – The protected 6-(diazomethyl)uracil **5** was prepared in two steps from the known carbaldehyde **3** [20] (*Scheme 1*). This aldehyde was first obtained in 66% yield by formylating **1** [21], but the SeO_2 oxidation of **2** [20] proved more convenient for the preparation of larger quantities of **3**, yielding 75% of **3** from **2** on a scale of 40 g. The (*E*)/(*Z*) ratio of the hydrazone **4**, but not the yield (82–84%) depends strongly upon the reaction conditions. A 3:1 (*E*)/(*Z*) mixture of **4** was obtained by using $NH_2NH_2 \cdot AcOH$ and K_2CO_3 in dry EtOH, and a 9:1 mixture by using $NH_2NH_2 \cdot H_2O$ and $NH_2NH_2 \cdot AcOH$ in 96% EtOH. Pure (*E*)-**4** was obtained by crystallisation of (*E*)/(*Z*)-**4** 9:1 from MeOH. The oxidation of (*E*)/(*Z*)-**4** with freshly prepared MnO_2 in DMSO led to impure **5** that decomposed in contact with silica gel. The analogous oxidation in CH_2Cl_2/DMSO 5:1, however, proceeded cleanly, yielding 90% (on a 4-g scale) of the 6-(diazomethyl)uracil **5** as a yellow solid that was pure according to ^{1}H- and ^{13}C-NMR spectroscopy, and was stored at room temperature for several days and at 5° for several weeks without any decomposition.

Scheme 1



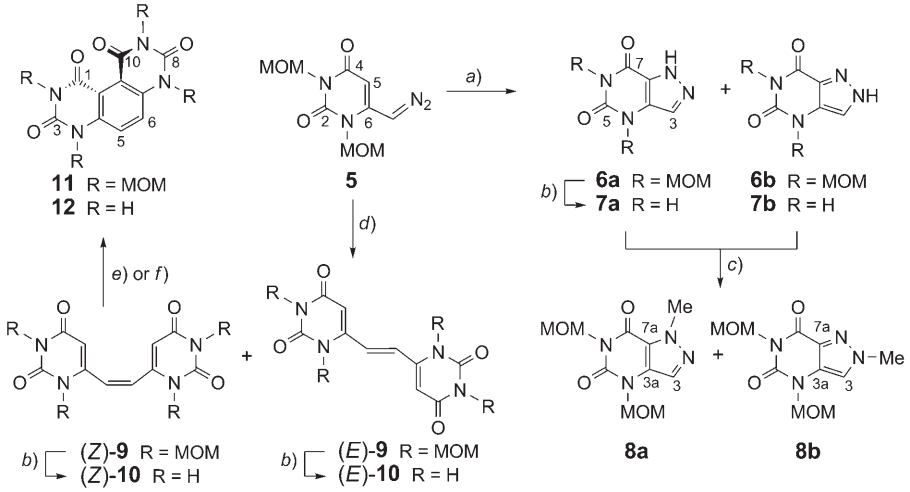
a) Lithium diisopropylamide (LDA), DMF, hexane/THF, −78°; 66%. *b*) SeO_2, 1,4-dioxane/AcOH 11:1, reflux; 75%. *c*) $NH_2NH_2 \cdot H_2O$, $NH_2NH_2 \cdot AcOH$, 96% EtOH, r.t.; 84%. *d*) MnO_2, CH_2Cl_2/DMSO 14:3, r.t.; 90%.

The assignment of the configuration of **4** is based on the characteristic downfield shift for the ^{1}H-NMR CH=N and NH_2 signals of the (*E*)-isomer [22] in $CDCl_3$ or in (D_6)DMSO ($\Delta\delta = 0.4-0.9$ ppm). Formation of the 6-(diazomethyl)uracil **5** is evidenced by the IR band at 2091 cm^{-1} and by the diagnostic high-field shift of the ^{1}H- and ^{13}C-NMR signals of the diazomethyl moiety (5.33 and 44.86 ppm, resp.; *cf.* [23]).

Thermolysis of the 6-(diazomethyl)uracil **5** in boiling toluene gave an equilibrating mixture **6a**/**6b** of annulated 1*H*- and 2*H*-pyrazoles (*Scheme 2*; *cf.* [24]). Sublimating crude **6a**/**6b** at 180° and 0.08 Torr resulted in 52% of **6a**/**6b** that was demethoxymethylated to **7a**/**7b** by treatment with BCl_3 in CH_2Cl_2 at −78° to room temperature [21]. Prolonged treatment (10 h at room temperature) with BCl_3 led to partial decomposition before deprotection was complete, while BBr_3 [25] removed both methoxy-

methyl (MOM) groups. Crystallization of the product from MeOH yielded 55% of **7a**/**7b** [26] that dissolved readily in DMSO to give a solution of a 1:1 mixture, sharp NH signals denoting that, under these conditions, the tautomers equilibrate slowly, if at all. We assume that equilibration is considerably impeded by the intermolecular H-bonds to the solvent that are evidenced by a strong downfield shift of the NH signals, resonating at 13.95 and 13.75 ppm. The mixture **6a**/**6b** was further characterized by methylation with NaH and MeI in DMSO, leading to a mixture of **8a** and **8b** that were separated by flash chromatography. Crystallization from 95% EtOH gave 54% of **8a** and 24% of **8b**.

Scheme 2



a) Toluene, 110°; 52% of **6a**/**6b**. *b*) BBr_3, CH_2Cl_2, −78° to r.t.; 55% of **7a**/**7b** 1:1; 52% of (*Z*)-**10**; 58% of (*E*)-**10**. *c*) NaH, MeI, DMSO; 54% of **8a** and 24% of **8b**. *d*) $Rh_2(OAc)_4$, CH_2Cl_2, r.t.; 45% of (*Z*)-**9**, 22% of (*E*)-**9**. *e*) I_2, $CHCl_3$, visible light; 32% of (*E*)-**9** and 10% of **11**, besides 48% of (*Z*)-**9**. *f*) 12N HCl, 95°; 73% of **12**.

The structure assignment to the pyrimidine diones **8a** and **8b** is based on the observation that imino C-atoms (as C(7a) in **8b**) resonate *ca.* 10 ppm downfield relative to corresponding enamino C-atoms [27]. Thus, C(3) of **8a** resonates downfield relative to C(3) of **8b** (123.81 *vs.* 116.22 ppm), and C(7a) of **8b** downfield to C(7a) of **8a** (130.68 *vs.* 119.70 ppm), whereas C(3a) of **8a** and **8b** resonate at a similar field (129.65 *vs.* 127.42 ppm). Accordingly, we assigned the ^{13}C-NMR signals of the (very) slowly equilibrating 1:1 mixture **7a**/**7b** in (D_6)DMSO as indicated in the *Exper. Part.* A rapidly equilibrating mixture **6a**/**6b** in $CDCl_3$ is evidenced by a single set of broad ^{13}C-NMR signals. Particularly broad are the signals of C(3) at 119.01 and of C(7a) at 127.9 ppm. In the ^{1}H-NMR spectrum of **7a**/**7b**, the more strongly shielded *s* at 7.42 ppm is assigned to H−C(3) of **7a** and that at 7.62 ppm to H−C(3) of **7b**, as suggested by a comparison with literature data [28]. The NH signals of **7a** and **7b** could not be assigned.

The Rh^{II}-promoted transformation of diazo compounds generates carbenoids that dimerize to alkenes in the absence of carbenophiles[2]). Treatment of **5** with 2 mol-% of $Rh_2(OAc)_4$ in CH_2Cl_2 [30–33] afforded a 3:1 mixture of (*Z*)-**9** and (*E*)-**9**. Crystallisation from AcOEt/hexane 1:1 gave 22% of (*Z*)-**9**, and flash chromatography of the mother liquor afforded an additional 23% of (*Z*)-**9** and 22% of (*E*)-**9**. Both (*Z*)-**9** and (*E*)-**9** were deprotected with BBr_3 in CH_2Cl_2 to the high-melting (*Z*)-**10** (52%) and (*E*)-**10** (58%; both decomposing at >260°). In contrast to (*Z*)-**10**, (*E*)-**10** proved particularly sensitive to air, and decomposed within a few hours at ambient temperature.

The assignment of the configurations of (*Z*)-**9** and (*E*)-**9** is based on the hypsochromic and weakly hypochromic UV absorption of (*Z*)-**9** (267 (log ε 3.99) *vs.* 319 nm (log ε 4.08) for (*E*)-**9**). Irradiation with visible light of a solution of (*Z*)-**9** and catalytic amounts of I_2 in $CHCl_3$ for 15 days at ambient temperature led to 32% of (*E*)-**9** and 10% of the pyrimidoquinazolinetetraone **11** (besides 48% of unreacted (*Z*)-**9**). The yield of the cyclisation/oxidation[3]) product **11** dropped to less than 5% when a boiling solution of (*Z*)-**9** was irradiated for 3 days. However, heating a solution of (*Z*)-**9** in 12N HCl to 95° gave exclusively the deprotected cyclisation/oxidation product **12** in 73% yield. Force-field calculations suggest that **11** and **12** adopt a helical conformation; the 1,10-carbonyl groups are moved out of the plane of the benzene ring (calculated C(10a)–C(10b)–C(1)–O torsion angle 28.7°). The helical conformation is corroborated by the crystal structure of a parent triphenylene-1,4,5,8,9,12-hexaone (torsion angle 32.7° [35]) and of angucyclinones (torsion angles 14–33° [36]), and in keeping with the hypsochromic shift of the UV bands of **11** (246 nm) and **12** (241 nm) as compared to (*Z*)-**9** (267 nm). The C_2 symmetry of **9**–**12** is evidenced by the single set of signals in the NMR spectra.

The addition of carbenoids to 3,4-dihydro-2*H*-pyran [29][30][37][38], 2,3-dihydrofuran [29][38–40], furan [31–33][40–43], and thiophene [33][40–45] is well precedented. Annulated cyclopropanes resulting from these reactions, were, as a rule, obtained as *endo*/*exo*-mixtures.

We investigated the addition of **5** to 3,4-dihydro-2*H*-pyran, 2,3-dihydrofuran, thiophene, furan, and (*E*)-2-styrylfuran; we also explored the *Lewis*-acid catalyzed vinylcyclopropane–cyclopentene rearrangement[4]) of the addition products.

The $Rh_2(OAc)_4$-catalyzed reaction of **5** with 3,4-dihydro-2*H*-pyran gave 78% of a 4:3 *endo*/*exo*-mixture of annulated cyclopropanes **13** that were partially separated by flash chromatography (*Scheme 3*). Treatment of a 4:3 mixture *endo*-**13**/*exo*-**13** with $AlCl_3$ in CH_2Cl_2 at 0° induced a vinylcyclopropane–cyclopentene rearrangement[5]) that led, *via* zwitterion **A**, in 88% yield to the 2-oxabicyclo[4.3.0]nona-pyrimidine **14**. Similarly, the $Rh_2(OAc)_4$-catalyzed reaction of **5** with 2,3-dihydrofuran gave 86% of a 2:1 *endo*/*exo*-mixture of annulated cyclopropanes **15**, which could not be separated by flash chromatography. Treatment of this mixture with Me_2AlCl in CH_2Cl_2/hexane gave the expected 2-oxabicyclo[3.3.0]octa-pyrimidine **16** (51%) besides the 5*H*-cyclo-

---

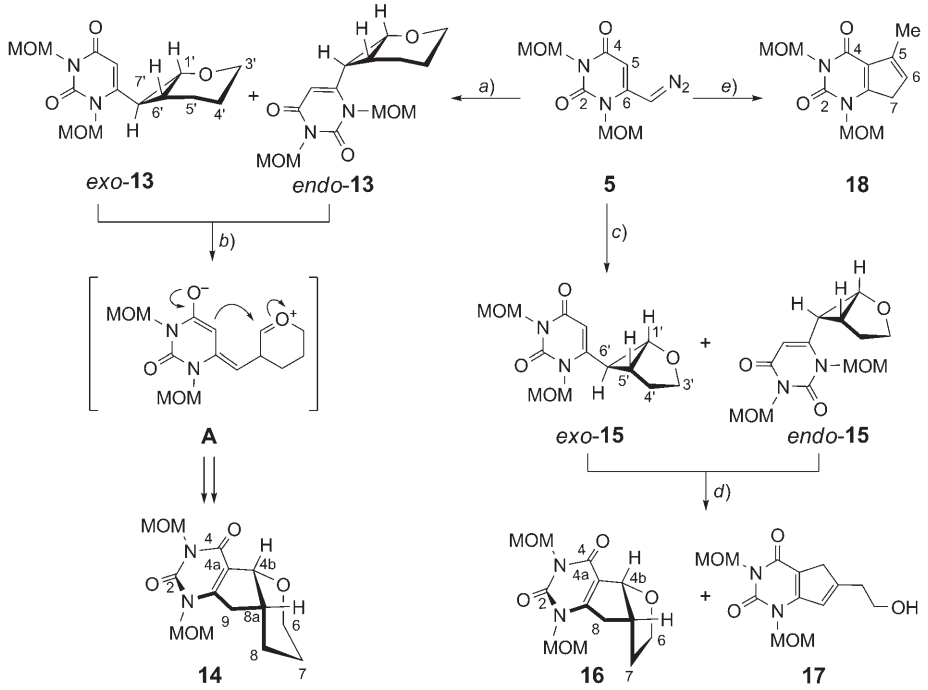
[2]) For the preparation of (*E*)- and (*Z*)-alkenes from cabenoids, see, *e.g.*, [29].

[3]) For reviews, see [34].

[4]) For reviews, see [46–48].

[5]) For vinylcyclopropane–cyclopentene rearrangements of 2-oxabicyclo[3.1.0]hexanes and 2-oxabicyclo[4.1.0]heptanes, see [49].

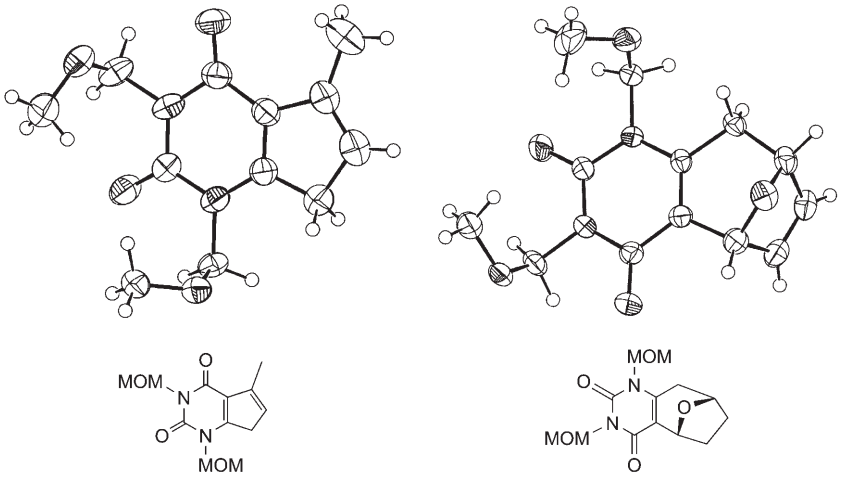
Scheme 3



a) $Rh_2(OAc)_4$, 3,4-dihydro-2*H*-pyran/CH_2Cl_2 1:3, r.t.; 78% of *endo*-**13**/*exo*-**13** 4:3. *b*) $AlCl_3$, CH_2Cl_2, 0°; 88%. *c*) $Rh_2(OAc)_4$, 2,3-dihydrofuran/CH_2Cl_2 2:15, r.t.; 86% of *endo*-**15**/*exo*-**15** 2:1. *d*) 1M Me_2AlCl in hexane, CH_2Cl_2, −78° to r.t.; 51% of **16** and 20% of **17**. *e*) $Rh_2(OAc)_4$, 2-methoxyprop-1-ene/CH_2Cl_2 2:3, r.t.; 1M Me_2AlCl in toluene, CH_2Cl_2, −78° to r.t.; 55%.

penta[*d*]pyrimidine **17** (20%). The position of the cyclopentene C=C bond of **17** is evidenced by a NOE of 10% for the vinyl H-atom resulting from irradiation of the N(1)CH_2 group. The formation of **17** from **16** involves the *Lewis*-acid catalyzed ring opening of the oxolane ring to form an *N*-acylimmonium cation, followed by deprotonation and isomerisation to the thermodynamically favoured **17** (linear dienone system). The $Rh_2(OAc)_4$-catalyzed reaction of **5** with 2-methoxyprop-1-ene led to a product, presumably an *endo*/*exo*-mixture of cyclopropanes, which was not analyzed, but treated with Me_2AlCl in CH_2Cl_2/hexane to yield 55% of the 7*H*-cyclopenta[*d*]pyrimidine **18**. The structure of **18** was established by X-ray crystal structure analysis (*Fig.*)[6]). Comparing the structure of **17** and **18** suggests that the degree of substitution determines the position of the cyclopentene C=C bond of **18** (hyperconjugation and linear *N*-acyl dienamine system). This hypothesis is supported

[6]) The crystallographic data have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC-671360 (**18**) and CCDC-671361 (**20**). Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB21EZ (fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk).



18 **20**

Figure. *X-Ray crystal structures of* **18** *and* **20**

by AM1 calculations according to which **17** and **18** are more stable by 2.69 and 1.86 kcal/mol, respectively, than their C=C bond isomers.

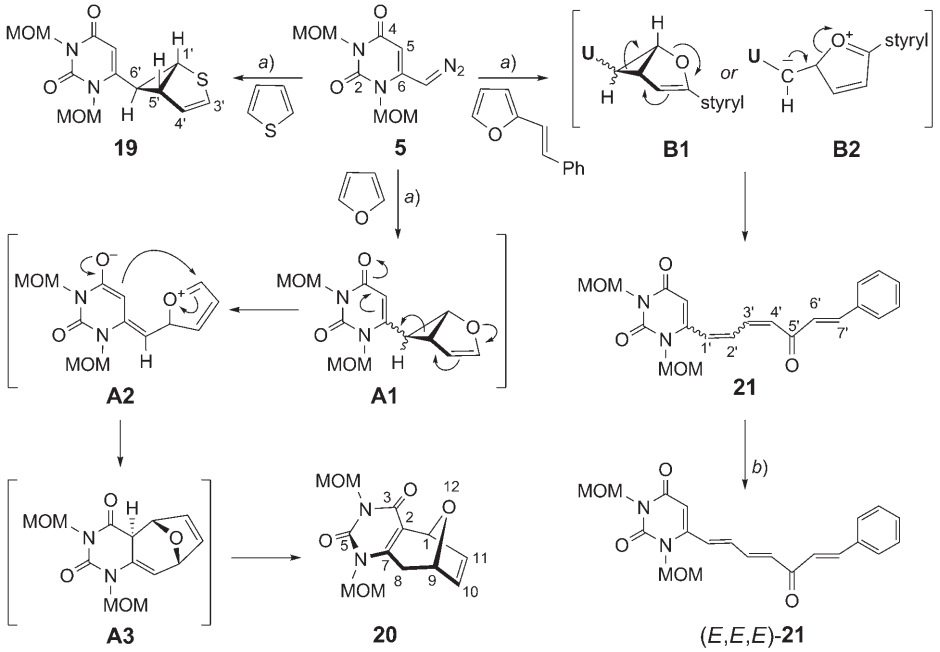
The $Rh_2(OAc)_4$-catalyzed reaction of **5** with thiophene gave selectively the *exo*-configured 2-thiabicyclo[3.1.0]hex-3-ene **19** (69%; *Scheme 4*). Neither Me_2AlCl nor $AlCl_3$ promoted a vinylcyclopropane–cyclopentane rearrangement, and **19** remained unaffected by these *Lewis* acids. In contradistinction, the $Rh_2(OAc)_4$-catalyzed reaction of **5** with furan led in 73% yield to the 8-oxabicyclo[3.2.1]octa-2,6-diene **20**[7]). Apparently, $Rh_2(OAc)_4$ catalyzed the formation of the 2-oxabicyclo[3.1.0]hex-3-ene **A1** and its fragmentation to the zwitterion **A2** which reacts *via* **A3** to **20**. The selective formation of the bridged rearrangement product **20** correlates with the far higher stability of the 2*H*-furanium cation **A2** than of the analogous 3*H*-furanium cation ($\Delta E = 16.47$ kcal/mol; AM1 calculation). The structure of **20** was established by X-ray crystal structure analysis (*Fig.*)[6]).

Finally, we explored the $Rh_2(OAc)_4$-catalyzed reaction of **5** with (*E*)-2-styrylfuran. It led exclusively to a mixture of diastereoisomeric hepta-1,4,6-trien-3-ones **21** (*Scheme 4*). A ^{1}H-NMR spectrum of the crude product showed four *s*s for H–C(5) of the uracil moiety, resonating at 5.75, 5.78, 6.01, and 5.96 ppm, and suggesting a *ca.* 50:26:20:4 mixture (*Z*,*Z*,*E*)-**21**/(*Z*,*E*,*E*)-**21**/(*E*,*E*,*E*)-**21**/(*E*,*Z*,*E*)-**21**. Flash chromatography (AcOEt/cyclohexane 2:1) gave a pure sample of (*Z*,*Z*,*E*)-**21** (6%) and a mixture of the four diastereoisomers of **21** (69%). Keeping a solution of this mixture in MeOH at ambient temperature for 7 d led to the complete disappearance of (*Z*,*Z*,*E*)-**21** in favour of (*E*,*E*,*E*)-**21**. Evaporation and crystallisation from AcOEt/hexane gave 60% of (*E*,*E*,*E*)-**21**.

---

[7]) For the preparation of 8-oxabicyclo[3.2.1]oct-2-enes from 2-oxabicyclo[3.1.0]hex-3-enes by electrocyclic ring opening and 1,3-dipolar cycloaddition, see [43].

Scheme 4



a) $Rh_2(OAc)_4$, CH_2Cl_2, r.t.; 69% of **19**; 73% of **20**; 6% of (*Z*,*Z*,*E*)-**21**, and 69% of a mixture of (*Z*,*Z*,*E*)-**21**, (*Z*,*E*,*E*)-**21**, (*E*,*E*,*E*)-**21**, and (*E*,*Z*,*E*)-**21**. *b*) MeOH, r.t.; 60%.

The formation of **21** is not unexpected, considering the synthesis of penta-2,4-dienals by the reaction of carbenoids with furans [31][32][40][41]. Addition of the carbenoid resulting from **5** to the unsubstituted C=C bond of the furanyl moiety may lead to the intermediate 2-oxabicyclo[3.1.0]hex-3-enes **B1**. Generation of a zwitterionic species **B2**, corresponding to **A2**, *via the* cyclopropanes **B1**, or directly from styrylfuran is not unlikely, even if no 8-oxabicyclo[3.2.1]octa-2,6-diene was obtained from styrylfuran, since a cyclisation similar to the one of **A2** may be disfavoured by the styryl substitutent of the intermediate **B2**. The cyclopropane **B1** may be transformed into **21** by a (concerted) ring opening, similar to the one observed for the *exo*-2-oxabicyclo[3.1.0]hex-3-enes derived from 2-methyl- and 2,5-dimethylfuran [31], with *endo*-**B1** leading to (*Z*,*Z*,*E*)-**21** and *exo*-**B1** to (*E*,*Z*,*E*)-**21**. However, the relative proportion of C=C bond isomers in the crude product requires that $\geq$76% of *endo*-**B1** be formed, and the 2-oxabicyclo[3.1.0]hex-3-enes **B1** appear, therefore, rather unlikely intermediates. We consider the 2*H*-furanium-2-methylide **B2** to be the relevant intermediate, and to lead to (*Z*,*Z*,*E*)-**21** and (*E*,*Z*,*E*)-**21**. An analogous intermediate was postulated as resulting from the addition of carbenoids to furan [31], considering that the corresponding *exo*-2-oxabicyclo[3.1.0]hex-3-ene proved stable under the reaction conditions [31][32].

The configuration of **13**–**16** was assigned on the basis of DQFCOSY, HSQC, and HMBC spectra. The *exo*- and *endo*-isomers of **13** and **15** are easily distinguished by the

value of the vicinal couplings constants that are larger for *cis*- than for *trans*-cyclopropanes (*Table*; *cf.* [29][31–33][41][50]). The O-substituent at C(1′) reduces the values for $J(1',7')$ of **13** and $J(1',6')$ of **15** (*cf.* [51]). The *endo*-isomers of **13** and **15** show an allylic coupling of 1.2–1.5 Hz between H–C(5) and H–C(7′ or 6′), whereas the *exo* isomers show at best a weak line broadening for these signals. The *cis*-annulation of **14** and **16** is evidenced by $J(4b,8a)$ of 4.5 and $J(4b,7a)$ of 7.8 Hz, respectively. The newly formed methylene group of **14** and **16** appears in the ^{1}H-NMR spectra as two *dd*s with a geminal coupling of 17.1 and 15.0 Hz, respectively. In the ^{13}C-NMR spectra, the *d* of C(4b) of **14** and **16** appears at 76.03 and 83.55 ppm, respectively, the *t* of C(9) of **14** at 33.37 ppm, and the *t* of C(8) of **16** at 37.17 ppm.

Table. *Vicinal Couplings* [Hz] *of the Cyclopropyl H-Atoms of* **13**, **15**, *and* **19**

	$J(1',7')$ of **13** *or* $J(1',6')$ of **15** and **19**	$J(6',7')$ of **13** *or* $J(5',6')$ of **15** and **19**	$J(1',6')$ of **13** *or* $J(1',5')$ of **15** and **19**
endo-**13**	6.6	9.9	6.0
exo-**13**	2.4	[a])	7.5
endo-**15**	5.7	9.0	5.3
exo-**15**	1.2	< 2.0	5.6
exo-**19**	3.6	3.9	7.5

[a]) Not assigned.

The *exo*-orientation of the pyrimidine moiety of **19** is evidenced by small $J(1',6')$ and $J(5',6')$ couplings of 3.6–3.9 Hz (*Table*; *cf.* [45]). These coupling contants are larger than those of *exo*-**15**, as expected from replacing the O- by an S-atom. H_{exo}–C(8) of **20** resonates as a *dd* at 3.11 ppm and H_{endo}–C(8) as a *d* at 2.31 ppm with J_{gem} of 18.0 Hz. The coupling of 6.0 Hz between H_{exo}–C(8) and H–C(9), and the absence of a coupling between H_{endo}–C(8) and H–C(9) agree well with the H–C–C–H torsion angles of −45 and 81° of the crystal structure and with the calculated coupling constants of 6.1 and 0.9 Hz. C(1), C(8), and C(9) of **20** resonate at 72.95, 25.82, and 76.38 ppm, respectively.

The assignment of the configuration of (*Z*,*Z*,*E*)-**21** and (*E*,*E*,*E*)-**21** is based on DQFCOSY, HSQC, and HMBC spectra. The two (*Z*)- and the (*E*)-configured C=C bonds of (*Z*,*Z*,*E*)-**21** are evidenced by $J(1',2') = J(2',3') = J(3',4') = 11.4–11.7$ Hz and $J(6',7') = 16.2$ Hz. Additionally, (*Z*,*Z*,*E*)-**21** shows *w* couplings of 0.9–1.2 Hz between H–C(5) and H–C(1′), between H–C(1′) and H–C(3′), and between H–C(2′) and H–C(4′), and a ^5J coupling of 1.2 Hz between H–C(1′) and H–C(4′). $J(3',4') = 15.3$ and $J(6',7') = 15.9$ Hz of (*E*,*E*,*E*)-**21** evidence two (*E*)-configured C=C bonds, whereas the higher-order signal of H–C(1′) and H–C(2′) at 7.06–6.93 ppm allows only estimation of the value of *ca.* 16 Hz for the large $J(1',2')$.

We thank Dr. *B. Schweizer* for the determination of the X-ray structures, and the *Swiss National Science Foundation* and *Syngenta*, Basel, for generos support.

Experimental Part

General. Flash chromatography (FC): *Merck* silica *60* (0.063–0.200 mm). UV Spectra: in MeOH, λ_{max} (log ε) in nm. FT-IR Spectra: neat (ATR); in cm^{-1}. HR-MALDI-MS: in 3-hydroxypicolinic acid (3-HPA) matrix. Force-field and semiempirical calculations were done with the programme Spartan 04 *Macintosh* from *Wavefunction Inc.*, Irvine, CA.

1,3-Bis(methoxymethyl)-6-methyluracil (**2**) [20]. A suspension of 6-methyluracil (30 g, 0.24 mol) in MeCN (300 ml) was treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 78 ml, 0.52 mol) and stirred at r.t. for 0.5 h. The clear soln. was cooled to 0°, treated dropwise with methoxymethyl chloride (MOMCl; 39.9 ml, 0.17 mol), stirred at r.t. for 3 d, and evaporated. The residue was diluted with H_2O (400 ml) and extracted with CH_2Cl_2 (4 × 50 ml). The combined org. layers were washed with brine (30 ml), dried (Na_2SO_4), and evaporated. FC (cyclohexane/AcOEt 2:1) gave **2** (34.1 g, 67%). M.p. 82.5–83.5° ([20]: 83–85°).

1,3-Bis(methoxymethyl)uracil-6-carbaldehyde (**3**) [20] *a*) *From* **1**. At −78°, a soln. of 2M soln. of LDA in hexane (4 ml, 7.95 mmol) in THF (11 ml) was treated dropwise with a soln. of **1** [21] (530 mg, 2.65 mmol) in dry THF (11 ml) over 10 min, stirred for 1 h, treated with DMF (2.2 ml, 11 mmol), stirred for 2.5 h, treated with AcOH (1.5 ml), and allowed to warm to 23°. The mixture was diluted with AcOEt and washed with H_2O. The aq. phase was extracted several times with $CHCl_3$. The org. layers were separately washed with sat. aq. $NaHCO_3$ soln., H_2O and brine, dried (Na_2SO_4), and evaporated. The AcOEt soln. contained less pure **3**. FC (hexane/AcOEt 1:1) gave **3** (400 mg, 66%).

b) *From* **2**. According to [20], a soln. of **2** (30.0 g, 0.14 mol) in dry 1,4-dioxane/AcOH 11:1 (495 ml) was treated with SeO_2 (46.8 g, 0.42 mol), kept for 6 h at reflux, cooled to r.t., diluted with toluene, treated with *Celite*, and stirred for another 0.5 h. The mixture was filtered through *Celite*. After evaporation of the filtrate, the residue was treated with H_2O (400 ml) and extracted with CH_2Cl_2 (5 × 40 ml). The combined org. layers were dried (Na_2SO_4) and evaporated. FC (cyclohexane/AcOEt 1:2) gave **3** (40.7 g, 75%). Syrup. R_f (AcOEt) 0.70.

1,3-Bis(methoxymethyl)uracil-6-carbaldehyde Hydrazone (**4**). *a*) A soln. of **3** (200 mg, 0.88 mmol) in dry EtOH (7 ml) was treated with $NH_2NH_2 \cdot AcOH$ (81 mg, 0.88 mmol), and Na_2CO_3 (93 mg, 0.88 mmol) and stirred for 2 h, whereupon a precipitate was formed. After evaporation at 35°, the residue was dissolved in $CHCl_3$ (10 ml), washed twice with sat. aq. $NaHCO_3$ soln. and twice with H_2O, dried (Na_2SO_4), and evaporated to give crude (*E*)/(*Z*)-**4** 3:1 (174 mg, 82%).

b) A soln. of **3** (10 g, 43.86 mmol) in 95% EtOH (600 ml) was treated with $NH_2NH_2 \cdot H_2O$ (11 ml, 219.3 mmol) and $NH_2NH_2 \cdot AcOH$ (4 g, 43.86 mmol), and stirred at r.t. for 24 h. A precipitate was gradually formed. After concentration and dilution with H_2O (100 ml), the solid was filtered off and washed with H_2O and EtOH. Crystallisation of the solid ((*E*)/(*Z*)-**4** 9:1; 8.9 g, 84%) from MeOH gave pure (*E*)-**4**. White solid. R_f (AcOEt) 0.30. M.p. 193.5–194.6°. UV: 223 (3.86), 277 (3.97), 327 (4.14). IR (ATR): 3360*w*, 3181*w*, 3082*w*, 2988*w*, 2938*w*, 2831*w*, 1688*m*, 1660*s*, 1644*s*, 1601*m*, 1529*m*, 1446*s*, 1423*s*, 1373*m*, 1354*m*, 1342*m*, 1318*m*, 1265*w*, 1190*m*, 1173*m*, 1145*m*, 1119*w*, 1095*s*, 1073*s*, 1021*m*, 973*w*, 910*s*, 894*s*, 871*m*, 845*m*, 778*m*, 766*m*, 736*w*. ^{1}H-NMR (300 MHz, $CDCl_3$; (*E*)/(*Z*) 3:1): (*E*)-isomer: 7.56 (*s*, CH=N); 6.88 (br. *s*, NH_2); 6.00 (*s*, H–C(5)); 5.32, 5.27 (2*s*, 2 CH_2N); 3.38, 3.35 (2*s*, 2 MeO); (*Z*)-isomer: 6.92 (*s*, CH=N); 6.48 (br. *s*, NH_2); 5.84 (*s*, H–C(5)); 5.29, 5.12 (2*s*, 2 CH_2N); 3.385, 3.36 (2*s*, 2 MeO). ^{1}H-NMR (300 MHz, (D_6)DMSO; (*E*)/(*Z*) 9:1): (*E*)-isomer: 8.27 (*s*, NH_2); 7.50 (*s*, CH=N); 5.89 (*s*, H–C(5)); 5.20, 5.05 (2*s*, 2 NCH_2O); 3.29, 3.25 (2*s*, 2 MeO); (*Z*)-isomer: 7.38 (*s*, NH_2); 6.80 (*s*, CH=N); 5.78 (*s*, H–C(5)); 5.27, 5.17 (2*s*, 2 NCH_2O); 3.285, 3.27 (2*s*, 2 MeO). ^{13}C-NMR (75 MHz, (D_6)DMSO; only (*E*) isomer): 161.42 (*s*, C(4)); 152.42 (*s*, C(2)); 149.85 (*s*, C(6)); 124.85 (*d*, *C*H=N); 93.54 (*d*, C(5)); 74.53, 71.47 (2*t*, 2 NCH_2O); 56.88, 56.03 (2*q*, 2 MeO). HR-EI-MS: 242.1016 (M^+, $C_9H_{14}N_4O_4^+$; calc. 242.1015).

6-(Diazomethyl)-1,3-bis(methoxymethyl)uracil (**5**). A suspension of (*E*)/(*Z*)-**4** 9:1 (4.0 g, 17.2 mmol) in DMSO (150 ml) was stirred at 50° until a clear soln. was obtained. The soln. was cooled to r.t., diluted with CH_2Cl_2 (700 ml), treated with MnO_2 (6.0 g, 66.08 mmol), stirred at r.t. for 10 h, treated with *Celite*, and stirred for another 0.5 h. After filtration through *Celite* (washing with CH_2Cl_2), the filtrate was washed with H_2O (3 × 300 ml) and brine (300 ml), dried (Na_2SO_4), and evaporated. The residue was dried under high vacuum to give crude **5** (3.57 g, 90%). Yellow solid (> 95% pure according

to ^{1}H- and ^{13}C-NMR spectroscopy). M.p. 93.8–94.8°. R_f (cyclohexane/AcOEt 1:1) 0.30. UV: 227 (4.34), 250 (4.28), 317 (4.28). IR (ATR): 3091*w*, 2996*w*, 2940*w*, 2832*w*, 2091*s*, 1694*m*, 1646*s*, 1581*s*, 1448*s*, 1436*s*, 1391*w*, 1369*w*, 1335*s*, 1316*m*, 1264*m*, 1242*w*, 1198*m*, 1188*m*, 1169*m*, 1142*w*, 1109*m*, 1093*s*, 1067*s*, 1026*m*, 1016*m*, 968*w*, 909*s*, 888*m*, 801*m*, 774*m*, 752*w*, 735*w*, 716*w*, 661*w*, 647*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.42 (*s*, H–C(5)); 5.38, 5.26 (2*s*, 2 NCH_2O); 5.33 (*s*, CH=N_2); 3.44, 3.41 (2*s*, 2 MeO). ^{13}C-NMR (75 MHz, $CDCl_3$): 161.31 (*s*, C(4)); 152.55 (*s*, C(2)); 148.47 (*s*, C(6)); 91.39 (*d*, C(5)); 75.51, 71.98 (2*t*, 2 NCH_2O); 57.69, 56.73 (2*q*, 2 MeO); 44.86 (*d*, CH=N_2). HR-EI-MS: 240.0855 (M^+, $C_9H_{12}N_4O_4^+$; calc. 240.0859). Anal. calc. for $C_9H_{12}N_4O_4$ (240.22): C 45.00, H 5.03, N 23.32; found: C 45.00, H 4.95, N 23.13.

*4,6-Bis(methoxymethyl)-pyrazolo[4,3-*d*]pyrimidine-5,7(1*H *and 2*H*)-dione* (**6a** and **6b**, resp.). A soln. of **5a** (500 mg, 4.13 mmol) in toluene (30 ml) was stirred at 110° for 6 h, concentrated to 10 ml, and cooled to r.t. The precipitate was filtered off and washed with toluene to give a slightly yellow solid (150 mg). After evaporation of the filtrate, FC ($CHCl_3$/MeOH 95:5) gave additional 120 mg of a solid. Sublimation of the combined solids at 180°/0.08 Torr gave **6a**/**6b** (261 mg, 52%). White solid. M.p. 184.5–185.0°. UV: 228 (3.78), 284 (3.70). IR (ATR): 3144*w*, 3120*w*, 2996*w*, 2934*m*, 2827*w*, 1706*m*, 1650*s* (br.), 1613*m*, 1605*m*, 1533*w*, 1491*w*, 1467*w*, 1449*w*, 1414*m*, 1401*w*, 1391*w*, 1369*w*, 1347*m*, 1303*m*, 1275*s*, 1198*m*, 1180*m*, 1091*s*, 1083*s*, 1038*m*, 964*m*, 946*m*, 916*m*, 904*m*, 879*m*, 800*s*, 783*m*, 752*s*, 695*s*, 666*m*, 634*w*, 621*w*. ^{1}H-NMR (300 MHz, $CDCl_3$; equilibrating mixture of **6a**/**6b**): 12.5 (br. *s*, NH); 7.73 (*s*, H–C(3)); 5.52, 5.40 (2*s*, 2 NCH_2O); 3.49, 3.42 (2*s*, 2 MeO). ^{13}C-NMR (75 MHz, $CDCl_3$, equilibrating mixture of **6a**/**6b**): 157.10 (*s*, C(7)); 151.41 (*s*, C(5)); 127.9 (br. *s*, C(7a)); 127.61 (*s*, C(3a)); 119.01 (br. *d*, C(3)); 77.04, 72.58 (2*t*, 2 NCH_2); 57.96, 56.91 (2*q*, 2 MeO). HR-EI-MS: 240.0855 (M^+, $C_9H_{12}N_4O_4^+$; calc. 240.0859). Anal. calc. for $C_9H_{12}N_4O_4$ (240.22): C 45.00, H 5.03, N 23.32; found: C 44.94, H 4.94, N, 23.18.

*Pyrazolo[4,3-*d*]pyrimidine-5,7(1*H *and 2*H*)-dione* (**7a** and **7b**, resp.) [26]. A soln. of **6** (110 mg, 0.46 mmol) in dry CH_2Cl_2 (66 ml) was cooled to −78°, treated dropwise with 1M BBr_3 in CH_2Cl_2 (5.5 ml), stirred for 5 h, and warmed gradually to r.t. The mixture was stirred at r.t. for 48 h, cooled to 0°, and treated with MeOH (10 ml). After evaporation and co-evaporation with MeOH (4 × 15 ml), a suspension of residue in MeOH (30 ml) was filtered. After evaporation of the filtrate, crystallisation from MeOH gave **7a**/**7b** 1:1 (38.3 mg, 55%). M.p. 265.0–266.0°. UV: 206 (4.11), 282 (3.55). IR (ATR): 3290*m*, 3221*m*, 3132*m*, 3072*w*, 2830*w*, 1686*s* (br.), 1615*m*, 1454*w*, 1432*m*, 1382*m*, 1353*w*, 1304*m*, 1295*m*, 1169*m*, 1146*m*, 1072*w*, 1010*w*, 953*w*, 844*m*, 787*s*, 745*m*, 708*s*, 645*m*, 631*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO; **7a**/**7b** 1:1): 13.95, 13.75 (2*s*, 2 NH); 11.08, 10.94, 10.85, 10.71 (4*s*, 4 NH); 7.62, 7.42 (2*s*, 2 H–C(3)). ^{13}C-NMR (75 MHz, (D_6)DMSO; **7a**/**7b** 1:1): 158.64 (*s*, C(7) of **7b**); 154.91 (*s*, C(7) of **7a**); 151.24 (*s*, C(5) of **7a** and **7b**); 131.26 (*s*, C(7a) of **7b**); 129.90 (*s*, C(3a) of **7a**); 127.18 (*s*, C(3a) of **7b**); 125.08 (*d*, C(3) of **7a**); 121.23 (*s*, C(7a) of **7a**); 113.80 (*d*, C(3) of **7b**). HR-EI-MS: 152.0334 (M^+, $C_5H_4N_4O_2^+$; calc. 152.0329).

Methylation of **6a**/**6b**. A suspension of NaH (65% NaH in mineral oil washed with hexane, 12 mg, 0.5 mmol) in dry DMSO (2 ml) was stirred for 15 min, treated with **6a**/**6b** (100 mg, 0.42 mmol), stirred for 45 min, treated dropwise with MeI (93 µl, 0.84 mmol), stirred for 3 h, and poured into ice-cold H_2O. After extraction with CH_2Cl_2, the combined org. layers were dried (Na_2SO_4) and evaporated. FC (hexane/AcOEt 2:1) and crystallisations from 95% EtOH gave **8a** (57 mg, 54%) and **8b** (25 mg, 24%).

*Data of 1-Methylpyrazolo[4,3-*d*]pyrimidine-5,7(1*H*)-dione* (**8a**). M.p. 116.4–117.4°. R_f (hexane/AcOEt 2:3) 0.40 (UV: dull blue). IR (ATR): 3115*w*, 3000*w*, 2953*w*, 2938*w*, 2830*w*, 1708*m*, 1665*s* (br.), 1595*m*, 1548*m*, 1535*m*, 1446*s*, 1432*s*, 1416*w*, 1377*w*, 1331*m*, 1313*s*, 1262*m*, 1235*w*, 1188*m*, 1168*m*, 1154*m*, 1089*s*, 1038*w*, 994*s*, 958*s*, 924*s*, 913*s*, 835*m*, 796*m*, 768*m*, 752*m*, 738*m*, 668*s*, 631*w*, 615*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.48 (*s*, H–C(3)); 5.47, 5.36 (2*s*, 2 NCH_2O); 4.22 (*s*, MeN); 3.47, 3.40 (2*s*, 2 MeO). ^{13}C-NMR (75 MHz, $CDCl_3$): 154.51 (*s*, C(7)); 151.21 (*s*, C(5)); 129.65 (*s*, C(3a)); 123.81 (*d*, C(3)); 119.70 (*s*, C(7a)); 76.29, 72.24 (2*t*, 2 NCH_2O); 57.66, 56.67 (2*q*, 2 MeO); 38.63 (*q*, MeN). HR-EI-MS: 254.1007 (M^+, $C_{10}H_{14}N_4O_4^+$; calc. 254.1015).

*Data of 2-Methylpyrazolo[4,3-*d*]pyrimidine-5,7(2*H*)-dione* (**8b**). M.p. 141.4–142°. R_f (hexane/AcOEt 2:3) 0.10 (UV: bright blue). IR (ATR): 3115*w*, 2936*w*, 2822*w*, 1713*m*, 1670*s*, 1603*m*, 1527*m*, 1445*m*, 1405*m*, 1303*m*, 1278*m*, 1181*m*, 1098*s*, 1081*s*, 937*s*, 906*s*, 752*m*, 699*s*, 660*m*, 606*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.41 (*s*, H–C(3)); 5.51, 5.31 (2*s*, 2 NCH_2O); 4.06 (*s*, MeN); 3.47, 3.38 (2*s*, 2 MeO). ^{13}C-NMR (75 MHz, $CDCl_3$): 157.24 (*s*, C(7)); 151.22 (*s*, C(5)); 130.68 (*s*, C(7a)); 127.42 (*s*, C(3a)); 116.22 (*d*, C(3)); 76.84, 72.23 (2*t*, 2 NCH_2O); 57.75, 56.67 (2*q*, 2 MeO); 40.72 (*q*, MeN). HR-EI-MS: 254.1007 (M^+, $C_{10}H_{14}N_4O_4^+$; calc. 254.1015).

Treatment of **5** *with* $Rh_2(OAc)_4$. A soln. of **5** (500 mg, 2.1 mmol) in dry CH_2Cl_2 (20 ml) was treated with $Rh_2(OAc)_4$ (9 mg, 0.02 mmol), stirred at r.t. under Ar for 20 min, and evaporated. The residue (crude (*Z*)/(*E*)-**9** *ca.* 3:1) was diluted with hexane/AcOEt 1:1 (15 ml) and stirred for 20 min. The solid was filtered off and washed with hexane/AcOEt 1:1 to give pure (*Z*)-**9** (101 mg). FC (cyclohexane/AcOEt 1:1 → 1:4 and then CH_2Cl_2/MeOH 10:1) of the mother liquor gave (*Z*)-**9** (106 mg; total yield: 45%) and (*E*)-**9** (98 mg, 22%).

*Data of (*Z*)-6,6′-(Ethene-1,2-diyl)bis[1,3-bis(methoxymethyl)uracil]* ((*Z*)-**9**). R_f (hexane/AcOEt 2:3) 0.40. M.p. 125.2–126.3°. UV: 228 (4.36), 267 (3.99). IR (ATR): 3091*w*, 3050*w*, 2965*w*, 2938*w*, 2829*w*, 1707*m*, 1651*s*, 1616*m*, 1447*s*, 1415*m*, 1373*m*, 1339*m*, 1314*m*, 1252*w*, 1194*m*, 1170*m*, 1143*m*, 1090*s*, 1018*m*, 973*w*, 912*m*, 869*m*, 808*w*, 776*m*, 760*w*, 737*w*, 700*w*, 680*w*, 643*w*, 609*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 6.78 (*s*, CH=CH); 5.62 (*s*, 2 H–C(5)); 5.35, 5.24 (2*s*, 4 NCH_2O); 3.46, 3.43 (2*s*, 4 MeO). ^{13}C-NMR (75 MHz, $CDCl_3$): 161.57 (*s*, 2 C(4)); 152.14 (*s*, 2 C(2)); 148.66 (*s*, 2 C(6)); 128.01 (*d*, *C*H=CH); 102.65 (*d*, 2 C(5)); 75.83, 72.29 (2*t*, 4 NCH_2O); 57.91, 57.32 (2*q*, 4 MeO). HR-EI-MS: 424.1589 (M^+, $C_{18}H_{24}N_4O_8^+$; calc. 424.1594). Anal. calc. for $C_{18}H_{24}N_4O_8$ (424.41; **9**/**10** *ca.* 3:1): C 50.94, H 5.70, N 13.20; found: C 51.00, H 5.68, N 13.09.

*Data of (*E*)-6,6′-(Ethene-1,2-diyl)bis[1,3-bis(methoxymethyl)uracil]* ((*E*)-**9**). R_f (hexane/AcOEt 2:3) 0.45. M.p. 234.5–235.3°. UV: 228 (4.39), 319 (4.08). IR (ATR): 3075*w*, 2991*w*, 2937*w*, 2830*w*, 1697*s*, 1650*s*, 1615*s*, 1484*w*, 1437*s*, 1411*s*, 1376*w*, 1352*m*, 1320*m*, 1262*w*, 1241*w*, 1196*m*, 1174*m*, 1147*s*, 1094*m*, 1082*s*, 1023*m*, 992*m*, 965*m*, 922*m*, 913*m*, 875*m*, 861*m*, 777*m*, 738*m*, 699*m*, 670*w*, 638*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.19 (*s*, CH=CH); 6.01 (*s*, 2 H–C(5)); 5.40, 5.27 (2*s*, 4 NCH_2O); 3.47, 3.46 (2*s*, 4 MeO). ^{13}C-NMR (75 MHz, $CDCl_3$): 161.74 (*s*, 2 C(4)); 152.10 (*s*, 2 C(2)); 149.57 (*s*, 2 C(6)); 128.28 (*d*, CH=CH); 101.66 (*d*, 2 C(5)); 75.86, 72.37 (2*t*, 4 NCH_2O); 58.07, 57.33 (2*q*, 4 MeO). HR-EI-MS: 424.1584 (M^+, $C_{18}H_{24}N_4O_8^+$; calc. 424.1594).

*(*Z*)-6,6′-(Ethene-1,2-diyl)diuracil* ((*Z*)-**10**). Under Ar, a soln. of (*Z*)-**9** (100 mg, 0.24 mmol) in dry CH_2Cl_2 (60 ml) was cooled to −78°, treated with 1M BBr_3 in CH_2Cl_2 (5.5 ml), stirred for 12 h, warmed gradually to r.t., stirred for 48 h, and treated dropwise with MeOH (10 ml). The soln. was stirred at 0° for 30 min. After evaporation and co-evaporation with MeOH (3 × 10 ml), a soln. of the residue in MeOH was neutralized with *Amberlite IR 93A* (OH^- form) and filtered (washing with MeOH). Evaporation of the filtrate gave (*Z*)-**10** (30.4 mg, 52%). M.p. >350° (dec.). IR (ATR): 3200*w* (sh), 3140*w*, 3090*w*, 3030*w*, 2806*w*, 1692*s*, 1666*s*, 1496*m*, 1440*m*, 1406*s*, 1332*w*, 1265*w*, 1053*m*, 1010*m*, 966*m*, 852*s*, 759*s*, 683*m*, 642*m*, 615*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 11.11 (*s*, 2 NH); 11.00 (*s*, 2 NH); 6.44 (*s*, CH=CH); 5.44 (*s*, 2 H–C(5)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 163.64 (*s*, 2 C(4)); 151.16 (*s*, 2 C(2)); 147.71 (*s*, 2 C(6)); 127.57 (*d*, CH=CH); 99.84 (*d*, 2 C(5)). HR-MALDI-MS: 271.0435 ($[M+Na]^+$, $C_{10}H_8N_4NaO_8^+$; calc. 271.0443).

*(*E*)-6,6′-(Ethene-1,2-diyl)diuracil* ((*E*)-**10**). Under Ar, a soln. of (*E*)-**9** (100 mg, 0.24 mmol) in dry CH_2Cl_2 (60 ml) was cooled to −78°, treated with 1M BBr_3 in CH_2Cl_2 (3.54 ml), stirred for 12 h, gradually warmed to r.t., and stirred for 48 h. After the dropwise addition of MeOH (8 ml) at 0°, the mixture was stirred at 0° for 30 min, evaporated, and co-evaporated with MeOH (3 × 10 ml). A soln. of the residue in MeOH (30 ml) was neutralized with *Amberlite IR 93A* (OH^- form) and filtered (washing with MeOH). Evaporation of the filtrate gave (*E*)-**10** (34 mg, 58%). M.p. >260° (dec.). IR (ATR): 3440*w* (br.), 3200*w* (sh), 3091*m*, 2991*m*, 2807*m*, 1697*s*, 1648*s* (br.), 1512*m*, 1439*s*, 1409*s*, 1365*m*, 1321*m*, 1238*w*, 1061*m*, 1021*w*, 968*m*, 855*m*, 760*s*, 710*m*, 662*m*, 638*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 11.18 (*s*, 2 NH); 11.01 (*s*, 2 NH); 7.11 (*s*, CH=CH); 5.62 (*s*, 2 H–C(5)).

Isomerisation of (*Z*)-**9**. A soln. of (*Z*)-**9** (500 mg, 1.18 mmol) in $CHCl_3$ (200 ml) was treated with I_2 (20 mg, 0.079 mmol) and irradiated with visible light (table lamp) at r.t. for 15 d. After evaporation, the residue was suspended in cyclohexane/AcOEt 1:1 (20 ml). The solid was filtered off and washed with cyclohexane/AcOEt 1:1 (5 ml) to give (*E*)-**9** (160 mg, 32%). Evaporation of the filtrate and FC (cyclohexane/AcOEt 2:1) gave (*Z*)-**9** (240 mg, 48%) and **11** (50 mg, 10%).

*Data of 2,4,7,9-Tetrakis(methoxymethyl)pyrimido[5,4-*f*]quinazoline-1,3,8,10-tetraone* (**11**). R_f (cyclohexane/AcOEt 1:1) 0.30. M.p. 234.5–235.0°. UV: 246 (4.49), 265 (sh). IR (ATR): 3109*w*, 2998*w*, 2933*w*, 2828*w*, 1732*m*, 1704*m*, 1664*s* (br.), 1576*w*, 1496*m*, 1482*s*, 1475*s*, 1451*m*, 1436*m*, 1415*s*, 1315*s*, 1307*s*, 1246*w*, 1201*w*, 1187*m*, 1177*m*, 1153*m*, 1145*m*, 1112*w*, 1079*s*, 1023*s*, 981*m*, 912*s*, 890*s*, 828*m*, 787*m*, 761*w*, 752*m*, 729*w*, 713*m*, 695*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.76 (*s*, H–C(5), H–C(6)); 5.58, 5.53 (2*s*, 4 NCH_2O);

3.52, 3.45 (2*s*, 4 MeO). ^{13}C-NMR (75 MHz, $CDCl_3$): 158.62 (*s*, C(1), C(10)); 150.87 (*s*, C(3), C(8)); 137.42 (*s*, C(4a), C(6a)); 122.06 (*d*, C(5), C(6)); 114.61 (*s*, C(10a), C(10b)); 75.40, 73.36 (2*t*, 4 NCH_2O); 58.09, 56.76 (2*q*, 4 MeO). HR-MALDI-MS: 461.1072 (10, $[M + K]^+$, $C_{18}H_{22}KN_4O_8^+$; calc. 461.1075), 445.1326 (31, $[M + Na]^+$, $C_{18}H_{22}N_4NaO_8^+$; calc. 445.1335), 423.1507 (100, $[M + H]^+$, $C_{18}H_{23}N_4O_8^+$; calc. 423.1510). Anal. calc. for $C_{18}H_{22}N_4O_8$ (422.39): C 51.18, H 5.25, N 13.26; found: C 51.53, H 5.04, N 12.94.

Pyrimido[5,4-f]quinazoline-1,3,8,10-tetraone (**12**). A soln. of (*Z*)-**9** (100 mg, 0.24 mmol) in 12N HCl (1 ml) was stirred at 95° for 8 h. The precipitate was filtered off and washed with H_2O (until pH 7) and MeOH. Drying gave yellow powdered **12** (43 mg, 73%). M.p. > 330° (dec.). UV: 203 (3.24), 241 (3.18). IR (ATR): 3350*w* (sh), 3261*m*, 3160*w*, 3019*m*, 2829*w*, 1656*s* (br.), 1503*m*, 1428*s*, 1291*m*, 1223*m*, 1208*m*, 1183*m*, 1055*m*, 1004*m*, 961*m*, 890*m*, 853*m*, 780*w*, 757*s*, 640*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 11.22 (*s*, 2 NH); 10.92 (*s*, 2 NH); 6.86 (*s*, H–C(5), H–C(6)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 162.92 (*s*, C(1), C(10)); 150.54 (*s*, C(3), C(8)); 143.39 (*s*, C(4a), C(6a)); 130.57 (*d*, C(5), C(6)); 108.68 (*s*, C(10a), C(10b)). HR-MALDI-MS: 247.0465 ($[M+H]^+$, $C_{10}H_7N_4O_4^+$; calc. 247.0462).

Reaction of **5** *with 3,4-Dihydro-2*H*-pyran.* A soln. of 3,4-dihydro-2*H*-pyran (20 ml) in CH_2Cl_2 (20 ml) was treated with $Rh_2(OAc)_4$ (40 mg, 8.4 μmol), stirred at r.t. for 30 min, treated dropwise with soln. of **5** (1.0 g, 4.16 mmol) in CH_2Cl_2 (40 ml), stirred at r.t. for 30 min, and evaporated. FC (CH_2Cl_2/AcOEt 4:1) gave *endo*-**13**/*exo*-**13** 4:3 (962 mg, 78%). FC (CH_2Cl_2/AcOEt 8:1) gave pure samples of *endo*-**13** and *exo*-**13**.

Data of endo-*1,3-Bis(methoxymethyl)-6-(2-oxabicyclo[4.1.0]heptan-7-yl)uracil* (*endo*-**13**). Syrup. R_f (cyclohexane/AcOEt 1:1) 0.33. UV: 208 (3.96), 271 (3.92). IR (ATR): 2940*w*, 2865*w*, 2830*w*, 1710*m*, 1660*s*, 1624*m*, 1432*s*, 1386*w*, 1359*m*, 1329*m*, 1307*m*, 1282*w*, 1235*w*, 1194*m*, 1171*w*, 1148*m*, 1124*m*, 1081*s*, 1053*m*, 1026*m*, 983*w*, 963*w*, 940*w*, 913*m*, 879*w*, 831*m*, 801*w*, 773*m*, 735*m*, 706*w*. ^{1}H-NMR (300 MHz, $CDCl_3$; assignments based on DQFCOSY, HSQC, and HMBC spectra): 5.98 (*d*, *J* = 1.2, H–C(5)); 5.47, 5.41 (2*d*, *J* = 10.8, CH_2–N(1)); 5.38 (*s*, CH_2–N(3)); 3.86 (*t*, *J* ≈ 6.3, H–C(1′)); 3.59 (br. *dt*, *J* = 10.5, 3.6, H_{eq}–C(3′)); 3.45 (*s*, *Me*OCH_2–N(3)); 3.41 (*s*, *Me*OCH_2–N(1)); 3.32 (*td*, *J* = 10.8, 2.7, H_{ax}–C(3′)); 2.08 (*ddt*, *J* ≈ 14.7, 11.7, 7.2, H_{ax}–C(5′)); 1.93 (br. *ddt*, *J* ≈ 14.7, 3.0, 1.5, H_{eq}–C(5′)); 1.86 (*ddd*, *J* = 9.9, 6.0, 1.5, H–C(7′)); 1.5–1.38 (*m*, H–C(6′)); 1.5–1.22 (*m*, 2 H–C(4′)). ^{13}C-NMR (75 MHz, $CDCl_3$; assignments based on a HSQC and a HMBC spectrum): 162.27 (*s*, C(4)); 153.04 (*s*, C(2)); 151.74 (*s*, C(6)); 104.73 (*d*, C(5)); 75.46 (*t*, CH_2–N(1)); 72.12 (*t*, CH_2–N(3)); 63.99 (*t*, C(3′)); 57.81 (*q*, *Me*OCH_2–N(3)); 57.11 (*q*, *Me*OCH_2–N(1)); 53.57 (*d*, C(1′)); 22.43 (*t*, C(4′)); 20.81 (*d*, C(7′)); 16.82 (*t*, C(5′)); 15.13 (*d*, C(6′)). HR-MALDI-MS: 319.1260 ($[M+Na]^+$, $C_{14}H_{20}N_2NaO_5^+$; calc. 319.1264). Anal. calc. for $C_{14}H_{20}N_2O_5$ (296.32): C 56.75, H 6.80, N 9.45; found: C 56.72, H 6.72, N 9.25.

Data of exo-*1,3-Bis(methoxymethyl)-6-(2-oxabicyclo[4.1.0]heptan-7-yl)uracil* (*exo*-**13**). Syrup. R_f (cyclohexane/AcOEt 1:1) 0.32. UV: 210 (3.99), 271 (3.99). IR (ATR): 2938*w*, 2860*w*, 2830*w*, 1711*m*, 1660*s*, 1623*m*, 1440*s*, 1385*w*, 1353*m*, 1337*m*, 1278*w*, 1254*w*, 1232*w*, 1195*m*, 1175*w*, 1136*m*, 1095*m*, 1082*s*, 1030*m*, 1013*m*, 989*w*, 969*m*, 913*m*, 868*w*, 855*w*, 817*w*, 781*m*, 772*m*, 727*s*, 667*w*, 646*w*, 617*w*. ^{1}H-NMR (300 MHz, $CDCl_3$; assignments based on DQFCOSY, HSQC, and HMBC spectra): 5.47, 5.40 (2*d*, *J* = 10.5, CH_2–N(1)); 5.32 (br. *s*, CH_2–N(3)); 5.30 (br. *s*, H–C(5)); 3.63 (*dd*, *J* = 7.5, 2.4, H–C(1′)); 3.63 (br. *dt*, *J* ≈ 10.5, 2.7, H_{eq}–C(3′)); 3.44 (*s*, *Me*OCH_2–N(1)); 3.40 (*s*, *Me*OCH_2–N(3)); 3.37 (*td*, *J* = 10.5, 6.3, H_{ax}–C(3′)); 2.06–2.00 (*m*, 2 H–C(5′), H–C(7′)); 1.58–1.51 (*m*, 2 H–C(4′), H–C(6′)). ^{13}C-NMR (75 MHz, $CDCl_3$; assignments based on a HSQC and a HMBC spectrum): 162.35 (*s*, C(4)); 154.80 (*s*, C(6)); 152.71 (*s*, C(2)); 98.18 (*d*, C(5)); 75.06 (*t*, CH_2–N(1)); 71.99 (*t*, CH_2–N(3)); 64.37 (*t*, C(3′)); 59.34 (*d*, C(1′)); 57.72 (*q*, *Me*OCH_2–N(3)); 57.02 (*q*, *Me*OCH_2–N(1)); 24.53 (*d*, C(7′)); 21.69 (*t*, C(4′)); 20.48 (*d*, C(6′)); 18.75 (*t*, C(5′)). HR-MALDI-MS: 319.1261 ($[M+Na]^+$, $C_{14}H_{20}N_2NaO_5^+$; calc. 319.1264).

cis-*1,3-Bis(methoxymethyl)-4b,6,7,8,8a,9-hexahydropyrano[2′,3′:3,4]cyclopenta[1,2-d]pyrimidine-2,4-dione* (**14**). A soln. of *endo*-**13**/*exo*-**13** 4:3 (500 mg, 1.69 mmol) in CH_2Cl_2 (25 ml) was cooled to 0°, treated with $AlCl_3$ (675 mg, 5.06 mmol), stirred for 3 h, treated with H_2O (30 ml), and extracted with CH_2Cl_2 (3 × 10 ml). The combined org. layers were neutralized with sat. $NaHCO_3$ soln., washed with brine, dried (Na_2SO_4), and evaporated. FC (cyclohexane/AcOEt 2:1) gave **14** (442 mg, 88%). Syrup. R_f (cyclohexane/AcOEt 2:1) 0.23. UV: 210 (3.91), 266 (3.91). IR (ATR): 2930*m*, 1715*s*, 1666*s*, 1636*m*, 1479*m*, 1090*s*, 1055*s*, 916*m*, 897*m*. ^{1}H-NMR (300 MHz, $CDCl_3$; assignments based on DQFCOSY, HSQC, and HMBC spectra): 5.41, 5.35 (2*d*, *J* = 9.6, CH_2–N(3)); 5.27, 5.14 (2*d*, *J* = 10.5, CH_2–N(1)); 4.76 (*d*, *J* = 4.5, H–C(4b)); 3.83 (br. *dt*, *J* ≈ 10.8, 2.1, H_{eq}–C(6)); 3.44 (*td*, *J* ≈ 11.1, 2.1, H_{ax}–C(6)); 3.44 (*s*,

*Me*OCH$_2$–N(3)); 3.43 (*s*, *Me*OCH$_2$–N(1)); 2.98 (*dd*, *J* = 17.1, 9.3, H$_a$–C(9)); 2.83 (*dd*, *J* = 17.1, 7.5, H$_b$–C(9)); 2.38–2.27 (*m*, H–C(8a)); 1.88 (*dt*, *J* ≈ 9.6, 4.5, 2 H–C(8)); 1.78–1.62 (*m*, H$_{ax}$–C(7)); 1.53 (br. *d*, *J* ≈ 13.2, H$_{eq}$–C(7)). ^{13}C-NMR (75 MHz, $CDCl_3$; assignments based on a HSQC and a HMBC spectrum): 159.83 (*s*, C(4)); 159.72 (*s*, C(9a)); 152.74 (*s*, C(2)); 114.09 (*s*, C(4a)); 76.09 (*t*, CH$_2$–N(1)); 76.03 (*d*, C(4b)); 72.17 (*t*, CH$_2$–N(3)); 65.28 (*t*, C(6)); 57.89 (*q*, *Me*OCH$_2$–N(3)); 57.36 (*q*, *Me*OCH$_2$–N(1)); 36.09 (*d*, C(8a)); 33.37 (*t*, C(9)); 23.73 (*t*, C(8)); 21.00 (*t*, C(7)). HR-MALDI-MS: 297.1446 ([*M* + H]$^+$, $C_{14}H_{21}N_2O_5^+$; calc. 297.1445). Anal. calc. for $C_{14}H_{20}N_2O_5$ (296.32): C 56.75, H 6.80, N 9.45; found: C 56.99, H 6.77, N 9.19.

endo- *and* exo-*1,3-Bis(methoxymethyl)-6-(2-oxabicyclo[3.1.0]hex-6-yl)uracil* (*endo*-**15** and *exo*-**15**). A soln. of 2,3-dihydrofuran (6 ml) in CH_2Cl_2 (15 ml) was treated with $Rh_2(OAc)_4$ (40 mg, 0.084 mmol), stirred at r.t. for 30 min, treated dropwise with soln. of **5** (1.0 g, 3.54 mmol) in CH_2Cl_2 (30 ml) for 30 min, and evaporated. FC (cyclohexane/AcOEt 1:4) gave *endo*-**15**/*exo*-**15** 2:1 (1.01 g, 86%). UV: 207 (3.27), 271 (3.27). IR (ATR): 2942*w*, 2895*w*, 2829*w*, 1711*m*, 1659*s*, 1622*m*, 1435*s*, 1382*w*, 1341*m*, 1308*w*, 1251*w*, 1195*m*, 1164*w*, 1145*w*, 1117*m*, 1082*s*, 1062*m*, 1025*m*, 965*m*, 912*m*, 883*m*, 834*m*, 817*m*, 783*w*, 771*m*, 756*m*, 693*w*, 661*w*. R_f (cyclohexane/AcOEt 1:3) 0.35. ^{1}H-NMR (300 MHz, $CDCl_3$; *endo*-**15**/*exo*-**15** 2:1): *endo*-**15**: 5.94 (*d*, *J* = 1.5, H–C(5)); 5.44 (*s*, CH$_2$–N(3)); 5.39, 5.32 (2*d*, *J* = 10.9, CH$_2$–N(1)); 4.27 (*t*, *J* = 5.5, H–C(1′)); 4.07 (*dt*, *J* = 9.5, 4.4, H$_a$–C(3′)); 3.45–3.39 (hidden by MeO signals, H$_b$–C(3′)); 3.44, 3.41 (2*s*, 2 MeO); 2.36–2.20, 2.19–2.10 (2*m*, H$_a$–C(4′), H–C(5′)); 1.98 (*ddd*, *J* = 13.1, 8.2, 4.1, H$_b$–C(4′)); 1.87 (*ddd*, *J* = 9.0, 5.3, 1.5, H–C(6′)); *exo*-**15**: 5.51, 5.35 (2*d*, *J* = 10.8, CH$_2$–N(1)); 5.37 (*s*, CH$_2$–N(3)); 5.31 (*s*, H–C(5)); 4.16 (*dt*, *J* = 9.1, 3.1, H$_a$–C(3′)); 4.00 (*dd*, *J* = 5.6, 1.2, H–C(1′)); 3.63 (*td*, *J* = 9.6, 7.8, H$_b$–C(3′)); 3.44, 3.42 (2*s*, 2 MeO); 2.36–2.20 (2 H), 2.19–2.10 (2*m*, 2 H–C(4′), H–C(6′)); 2.06 (br. *dd*, *J* = 10.3, 5.3, H–C(5′)). ^{13}C-NMR (75 MHz, $CDCl_3$; *endo*-**15**/*exo*-**15** 2:1): *endo*-**15**: 162.22 (*s*, C(4)); 153.63 (*s*, C(2)); 151.06 (*s*, C(6)); 103.63 (*d*, C(5)); 75.25 (*t*, CH$_2$–N(1)); 72.11 (*t*, CH$_2$–N(3)); 71.20 (*t*, C(3′)); 63.26 (*d*, C(1′)); 57.78 (*q*, *Me*OCH$_2$–N(3)); 57.04 (*q*, *Me*OCH$_2$–N(1)); 26.18 (*t*, C(4′)); 24.60 (*d*, C(6′)); 23.56 (*d*, C(5′)); *exo*-**15**: 162.11 (*s*, C(4)); 152.95 (*s*, C(6)); 152.65 (*s*, C(2)); 98.67 (*d*, C(5)); 74.99 (*t*, CH$_2$–N(1)); 72.03 (*t*, CH$_2$–N(3)); 67.45 (*t*, C(3′)); 66.67 (*d*, C(1′)); 57.78 (*q*, *Me*OCH$_2$–N(3)); 57.04 (*q*, *Me*OCH$_2$–N(1)); 27.75 (*t*, C(4′)); 24.66 (*d*, C(6′)); 22.02 (*d*, C(5′)). HR-ESI-MS: 305.1114 ([*M* + Na]$^+$, $C_{13}H_{18}N_2NaO_5^+$; calc. 305.1113). 282.0868 (*M*$^+$, $C_{13}H_{18}N_2O_5^+$; calc. 282.1216). Anal. calc. for $C_{13}H_{18}N_2O_5$ (282.3): C 55.31, H 6.43, N 9.92; found: C 54.89, H 6.43, N 9.72.

Lewis *Acid-Catalyzed Rearrangement of* endo-**15**/exo-**15**. A soln. of *endo*-**15**/*exo*-**15** 2:1 (200 mg, 0.71 mmol) in CH_2Cl_2 (5 ml) was cooled to −78°, treated with 1M Me_2AlCl in hexane (1.42 ml), stirred for 10 h, warmed gradually to r.t., and stirred for 24 h. The mixture was diluted with H_2O, neutralized with sat. $NaHCO_3$ soln., and extracted with CH_2Cl_2 (3 × 10 ml). The combined org. layer were washed with brine, dried (Na_2SO_4), and evaporated. FC (AcOEt/acetone/cyclohexane 1:1:0.5) gave **16** (101 mg, 51%) and **17** (40 mg, 20%). HR-ESI-MS: 305.1108 ([*M* + Na]$^+$, $C_{13}H_{18}N_2NaO_5^+$; calc. 305.1113). Anal. calc. for $C_{13}H_{18}N_2O_5$ (282.30): C 55.31, H 6.43, N 9.92; found: C 54.89, H 6.43, N 9.72.

Data of cis-*1,3-Bis(methoxymethyl)-6,7,7a,8-tetrahydro-1*H-*furo[2′,3′:3,4]cyclopenta[1,2-*d*]pyrimidine-2,4-dione* (**16**). Syrup. R_f (AcOEt/acetone/cyclohexane 1:1:0.5) 0.42. UV: 210 (3.92), 263 (3.86). IR (ATR): 2942*w*, 2830*w*, 1714*m*, 1663*s*, 1472*s*, 1392*w*, 1351*m*, 1330*m*, 1281*w*, 1175*m*, 1120*m*, 1075*s*, 1029*m*, 989*m*, 951*m*, 913*s*, 860*m*, 798*w*, 770*m*, 727*w*, 705*w*, 647*w*. ^{1}H-NMR (300 MHz, $CDCl_3$; assignments based on DQFCOSY, HSQC, and HMBC spectra): 5.37, 5.32 (2*d*, *J* = 9.3, CH$_2$–N(3)); 5.365 (*d*, *J* = 7.8, H–C(4b)); 5.18, 5.12 (2*d*, *J* = 10.8, CH$_2$–N(1)); 3.86 (*ddd*, *J* = 9.0, 6.6, 3.9, H$_a$–C(6)); 3.65 (*td*, *J* ≈ 6.0, 5.4, H$_b$–C(6)); 3.41 (*s*, *Me*OCH$_2$–N(3)); 3.38 (*s*, *Me*OCH$_2$–N(1)); 3.23–3.06 (*m*, H–C(7a), H$_a$–C(8)); 2.71 (*dd*, *J* = 15.0, 2.1, H$_b$–C(8)); 2.20–2.07 (*m*, H$_a$–C(7)); 1.73–1.68 (*m*, H$_b$–C(7)). ^{13}C-NMR (75 MHz, $CDCl_3$; assignments based on a HSQC and a HMBC spectrum): 159.87 (*s*, C(4)); 156.43 (*s*, C(8a)); 152.83 (*s*, C(2)); 111.51 (*s*, C(4a)); 83.55 (*d*, C(4b)); 75.70 (*t*, CH$_2$–N(1)); 72.09 (*t*, CH$_2$–N(3)); 66.60 (*t*, C(6)); 57.83 (*q*, MeOCH$_2$–N(3)); 57.18 (*q*, MeOCH$_2$–N(1)); 38.68 (*d*, C(7a)); 37.17 (*t*, C(8)); 34.35 (*t*, C(7)). HR-MALDI-MS: 305.1107 (96, [*M* + Na]$^+$, $C_{13}H_{18}N_2NaO_5^+$; calc. 305.1113), 283.1285 (100, [*M* + H]$^+$, $C_{13}H_{19}N_2O_5^+$; calc. 283.1294).

*Data of 6-(2-Hydroxyethyl)-1,3-bis(methoxymethyl)cyclopenta[*d*]pyrimidine-2,4(5*H*)-dione* (**17**). Solid. R_f (AcOEt/acetone/cyclohexane 1:1:0.5) 0.30. M.p. 101–102°. UV: 215 (4.03), 233 (4.06), 309 (3.85). IR (ATR): 3432*w*, 2937*w*, 2828*w*, 1687*s*, 1643*s*, 1547*m*, 1487*s*, 1469*s*, 1446*m*, 1433*m*, 1383*m*, 1363*m*, 1341*m*, 1322*m*, 1272*m*, 1240*m*, 1223*m*, 1188*m*, 1174*m*, 1148*m*, 1126*m*, 1093*s*, 1069*s*, 1041*m*, 1010*s*, 952*m*,

941*m*, 914*s*, 885*m*, 874*m*, 804*m*, 767*s*, 756*m*, 697*m*, 675*m*. ^{1}H-NMR (300 MHz, $CDCl_3$; assignments based on DQFCOSY, HSQC, and HMBC spectra): 6.50 (*s*, irrad. at 5.33 → NOE of 10%, H–C(7)); 5.41 (*s*, CH_2–N(3)); 5.33 (*s*, irrad. at 6.50 → NOE of 2%, CH_2–N(1)); 3.89 (*q*, *J* = 6.3, C*H*$_2$OH); 3.45 (*s*, H_2C(5)); 3.43 (*s*, *Me*OCH$_2$–N(3)); 3.40 (*s*, *Me*OCH$_2$–N(1)); 2.79 (*t*, *J* = 6.3, C*H*$_2$CH$_2$OH); 2.04 (br. *s*, OH). ^{13}C-NMR (75 MHz, $CDCl_3$; assignments based on a HSQC and a HMBC spectrum): 160.26 (*s*, C(6)); 159.01 (*s*, C(4)); 155.22 (*s*, C(7a)); 153.13 (*s*, C(2)); 120.96 (*d*, C(7)); 109.93 (*s*, C(4a)); 75.78 (*t*, CH_2–N(1)); 72.08 (*t*, CH_2–N(3)); 61.28 (*t*, CH_2OH); 57.59 (*q*, *Me*OCH$_2$–N(3)); 56.92 (*q*, *Me*OCH$_2$–N(1)); 39.36 (*t*, C(5)); 34.61 (*t*, C*H*$_2$CH$_2$OH). HR-MALDI-MS: 305.1106 (100, $[M + Na]^+$, $C_{13}H_{18}N_2NaO_5^+$; calc. 305.1113), 283.1285 (76, $[M + H]^+$, $C_{13}H_{19}N_2O_5^+$; calc. 283.1294), 251.1021 (97, $[M - CH_2OH]^+$, $C_{12}H_{15}N_2O_4^+$; calc. 251.2580). Anal. calc. for $C_{13}H_{18}N_2O_5$ (282.30): C 55.31, H 6.43, N 9.92; found: C 55.40, H 6.44, N 9.85.

*1,3-Bis(methoxymethyl)-5-methylcyclopenta[*d*]pyrimidine-2,4-(7H)-dione* (**18**). A soln. of 2-methoxyprop-1-ene (20 ml) in CH_2Cl_2 (10 ml) was treated with $Rh_2(OAc)_4$ (40 mg, 0.084 mmol), stirred at r.t. for 30 min, treated dropwise with a soln. of **5** (1.0 g, 4.3 mmol) in CH_2Cl_2 (20 ml), stirred for 30 min and evaporated. A soln. of the residue in CH_2Cl_2 (25 ml) was cooled to −78°, treated with 1M Me_2AlCl in toluene (7.05 ml), and stirred for 10 h at −78° and for 24 h at r.t. Evaporation and FC (AcOEt/cyclohexane 5:1) gave **18** (0.57 g, 55%). Colourless crystals. R_f (AcOEt/cyclohexane 5:1) 0.72. M.p. 124.7–125.0°. UV: 214 (3.84), 243 (3.90), 312 (3.45). IR (ATR): 2953*w*, 2892*w*, 2835*w*, 1702*m*, 1659*s*, 1582*m*, 1522*w*, 1493*m*, 1475*m*, 1445*m*, 1428*w*, 1413*m*, 1397*w*, 1368*m*, 1327*w*, 1305*m*, 1260*w*, 1237*w*, 1199*m*, 1176*m*, 1138*m*, 1117*m*, 1091*s*, 1070*s*, 1033*m*, 1008*m*, 983*m*, 956*w*, 922*s*, 909*s*, 877*w*, 779*m*, 757*m*, 740*m*, 701*m*, 650*m*, 621*s*. ^{1}H-NMR (300 MHz, $CDCl_3$; assignments based on DQFCOSY, HSQC, and HMBC spectra): 5.69 (br. *sext.*, *J* = 1.8, H–C(6)); 5.43 (*s*, CH_2–N(3)); 5.29 (*s*, CH_2–N(1)); 3.46 (*s*, *Me*OCH$_2$–N(3)); 3.41 (*s*, *Me*OCH$_2$–N(1)); 3.39 (br. *quint.*, *J* = 2.1, 2 H–C(7)); 2.24 (br. *q*, *J* = 2.1, Me). ^{13}C-NMR (75 MHz, $CDCl_3$; assignments based on a HSQC and a HMBC spectrum): 159.29 (*s*, C(4)); 157.63 (*s*, C(7a)); 152.33 (*s*, C(2)); 139.40 (*s*, C(5)); 118.63 (*d*, C(6)); 116.44 (*s*, C(4a)); 76.05 (*t*, CH_2–N(1)); 72.11 (*t*, CH_2–N(3)); 57.68 (*q*, *Me*OCH$_2$–N(3)); 57.09 (*q*, *Me*OCH$_2$–N(1)); 37.05 (*t*, C(7)); 15.09 (*q*, Me). HR-ESI-MS: 275.1003 ($[M + Na]^+$, $C_{12}H_{16}N_2NaO_4^+$; calc. 275.1008). Anal. calc. for $C_{12}H_{16}N_2O_4$ (252.27): C 57.13, H 6.39, N 11.10; found: C 57.25, H 6.36, N 10.96.

X-Ray Analysis of **18**[6]. Slow evaporation of a soln. of **18** in MeOH gave a single crystal suitable for X-ray-analysis (0.36 × 0.08 × 0.04 mm; colourless). $C_{12}H_{16}N_2O_4$ (252.270): monoclinic $P2_1$; *a* = 4.3736(3), *b* = 18.3636(11), *c* = 14.9891(12) Å, *β* = 94.117(4)°, V = 1200.74(15) Å^3; *Z* = 4, D_{calc} = 1.396 Mg/m^3. Intensities were measured on a *Nonius Kappa CCD* diffractometer, with MoK_α radiation (*λ* = 0.71073 Å, *θ* = 2.167–24.713°, μ = 0.106 mm^{-1}) at 223 K. Of the total 7129 reflections 2026 are independent and 1573 were observed. *R* = 0.1535, R_w = 0.3799.

exo-*1,3-Bis(methoxymethyl)-6-(2-thiabicyclo[3.1.0]hex-3-en-6-yl)uracil* (**19**). A soln. of thiophene (10 ml) and $Rh_2(OAc)_4$ (40 mg, 0.084 mmol) in CH_2Cl_2 (10 ml) was stirred at r.t. for 30 min, treated dropwise with a soln. of **5** (1.0 g, 4.16 mmol) in CH_2Cl_2 (20 ml), stirred for 2 h, and evaporated. FC (AcOEt/cyclohexane 2:1) gave **19** (0.85 g, 69%). Syrup. R_f (AcOEt/cyclohexane 2:1) 0.40. UV: 203 (4.01), 266 (3.99), 295 (3.91). IR (ATR): 3169*w*, 3019*w*, 2923*w*, 1713*w*, 1598*w*, 1495*w*, 1424*w*, 1331*w*, 1155*s*, 1120*s*, 1053*m*, 1032*s*, 1007*s*, 918*m*, 813*s*, 773*m*, 708*m*, 679*s*. ^{1}H-NMR (300 MHz, $CDCl_3$; assignments based on DQFCOSY, HSQC, and HMBC spectra): 6.20 (*dd*, *J* = 6.0, 1.5, H–C(3′)); 5.91 (*dd*, *J* = 5.7, 3.0, H–C(4′)); 5.39, 5.31 (2*d*, *J* = 10.5, CH_2–N(1)); 5.34, 5.30 (2*d*, *J* = 10.8, CH_2–N(3)); 5.30 (*s*, H–C(5)); 3.40 (*s*, *Me*OCH$_2$–N(1)); 3.39 (*s*, *Me*OCH$_2$–N(3)); 3.27 (*ddd*, *J* = 7.5, 3.6, 1.5, H–C(1′)); 2.96 (br. *dt*, *J* ≈ 7.2, 3.0, H–C(5′)); 1.52 (*t*, *J* = 3.9, H–C(6′)). ^{13}C-NMR (75 MHz, $CDCl_3$; assignments based on a HSQC and a HMBC spectrum): 161.93 (*s*, C(4)); 155.46 (*s*, C(6)); 152.46 (*s*, C(2)); 128.27 (*d*, C(3′)); 122.72 (*d*, C(4′)); 97.16 (*d*, C(5)); 74.95 (*t*, CH_2–N(1)); 71.99 (*t*, CH_2–N(3)); 57.71 (*q*, *Me*OCH$_2$–N(3)); 56.98 (*q*, *Me*OCH$_2$–N(1)); 38.75 (*d*, C(5′)); 34.62 (*d*, C(1′)); 23.05 (*d*, C(6′)). HR-MALDI-MS: 319.0726 (100, $[M + Na]^+$, $C_{13}H_{16}N_2NaO_4^+$; calc. 319.0728), 297.0905 (21, $[M + H]^+$, $C_{13}H_{17}N_2O_4S^+$; calc. 297.0909).

4,6-Bis(methoxymethyl)-12-oxa-4,6-diazatricyclo[7.2.1.0^{2,7}]dodeca-2(7),10-diene-3,5-dione (**20**). A soln. of furan (10 ml) and $Rh_2(OAc)_4$ (30 mg, 0.063 mmol) in CH_2Cl_2 (10 ml) was stirred at r.t. for 30 min, treated dropwise with a soln. of **5** (1.0 g, 4.16 mmol) in CH_2Cl_2 (20 ml), stirred at r.t for 2 h, and evaporated. FC (AcOEt/cyclohexane 2:1) gave **20** (917 mg, 73%). Colourless crystals. R_f (AcOEt/cyclohexane 2:1) 0.22. M.p. 122.0–122.5°. UV: 219 (4.01), 279 (3.82). IR (ATR): 2972*w*, 2940*w*, 2826*w*,

1692*m*, 1645*s*, 1585*w*, 1519*w*, 1462*s*, 1445*s*, 1428*m*, 1415*m*, 1390*w*, 1363*m*, 1334*m*, 1321*m*, 1280*w*, 1268*m*, 1250*w*, 1223*m*, 1211*w*, 1175*s*, 1110*s*, 1094*s*, 1070*s*, 1054*s*, 1020*m*, 1008*m*, 978*s*, 963*m*, 943*m*, 903*s*, 879*m*, 831*m*, 820*m*, 777*s*, 760*m*, 721*s*, 700*s*, 655*m*, 621*s*. ^{1}H-NMR (300 MHz, $CDCl_3$; assignments based on DQFCOSY, HSQC, and HMBC spectra): 6.61 (*dd*, $J = 5.7$, 1.5, H–C(11)); 6.03 (*dd*, $J = 5.7$, 1.5, H–C(10)); 5.49 (*d*, $J = 1.5$, H–C(1)); 5.39, 5.35 (2*d*, $J = 9.3$, CH_2–N(4)); 5.24, 5.19 (2*d*, $J = 10.8$, CH_2–N(6)); 5.10 (*dd*, , $J = 6.0$, 1.5, H–C(9)); 3.42 (*s*, *Me*OCH_2–N(4)); 3.37 (*s*, *Me*OCH_2–N(6)); 3.11 (*dd*, $J = 18.0$, 6.0, H_{exo}–C(8)); 2.31 (*d*, $J = 18.0$, H_{endo}–C(8)). ^{13}C-NMR (75 MHz, $CDCl_3$; assignments based on a HSQC and a HMBC spectrum): 159.82 (*s*, C(3)); 152.30 (*s*, C(5)); 145.63 (*s*, C(7)); 138.00 (*d*, C(11)); 127.73 (*d*, C(10)); 113.79 (*s*, C(2)); 76.38 (*d*, C(9)); 73.77 (*t*, CH_2–N(6)); 72.95 (*d*, C(1)); 72.12 (*t*, CH_2–N(4)); 57.86 (*q*, *Me*OCH_2–N(4)); 57.14 (*q*, *Me*OCH_2–N(6)); 25.82 (*t*, C(8)). HR-ESI-MS: 303.0952 ($[M + Na]^+$, $C_{13}H_{16}N_2NaO_5^+$; calc. 303.0957). Anal. calc. for $C_{13}H_{16}N_2O_5$ (280.28): C 55.71, H 5.75, N 9.99; found: C 55.72, H 5.78, N 9.99.

X-Ray Analysis of **20**[6]). Slow evaporation of a soln. of **20** in MeOH gave a single crystal suitable for X-ray-analysis ($0.34 \times 0.2 \times 0.08$ mm; colourless). $C_{13}H_{16}N_2O_5$ (280.280), orthorhombic $Pc2_1b$; $a =$ 4.6614(2), $b = 16.1141(8)$, $c = 17.3301(8)$, $V = 1301.74(10)$ Å^3; $Z = 4$, $D_{calc} = 1.430$ Mg/m^3. Intensities were measured on a *Nonius Kappa CCD* diffractometer, with MoK_α radiation ($\lambda = 0.71073$ Å, $\theta =$ 2.425–27.485°, $\mu = 0.111$ mm^{-1}) at 223 K. Of the total 2797 reflections 2583 are independent and 2243 were observed. $R = 0.0542$, $R_w = 0.1336$.

Reaction of **5** *with* (E)*-2-Styrylfuran.* A soln. of (*E*)-2-styrylfuran (0.85 g, 4.99 mmol) in CH_2Cl_2 (20 ml) was treated with $Rh_2(OAc)_4$ (40 mg, 0.084 mmol), stirred at r.t. for 30 min, treated dropwise with a soln. of **5** (1.0 g, 4.16 mmol) in CH_2Cl_2 (20 ml), stirred at r.t. for 1 h, and evaporated. A ^{1}H-NMR spectrum of the crude product suggested a 50 : 26 : 20 : 4 mixture (*Z*,*Z*,*E*)-**21**/(*Z*,*E*,*E*)-**21**/(*E*,*E*,*E*)-**21**/(*E*,*Z*,*E*)-**21**. FC (AcOEt/cyclohexane 2 : 1) gave pure (*Z*,*Z*,*E*)-**21** (100 mg, 6%) and a mixture of all four isomers of **21** (1.6 g, 69%).

*Data of 1,3-Bis(methoxymethyl)-6-[(1*Z*,3*Z*,6*E*)-5-oxo-7-phenylhepta-1,3,6-trien-1-yl]uracil* ((*Z*,*Z*,*E*)-**21**). Yellow solid. R_f (AcOEt/cyclohexane 3 : 1) 0.70. M.p. 164.0° (dec.). UV: 202 (4.34), 228 (4.25), 332 (4.47). IR (ATR): 3089*w*, 2981*w*, 2920*w*, 2828*w*, 1712*m*, 1662*s*, 1619*s*, 1590*m*, 1573*m*, 1494*w*, 1449*m*, 1433*m*, 1423*m*, 1413*m*, 1389*m*, 1360*m*, 1342*m*, 1323*m*, 1253*m*, 1228*m*, 1192*s*, 1170*m*, 1142*m*, 1093*s*, 1076*s*, 1048*m*, 1017*m*, 999*m*, 975*m*, 966*m*, 906*s*, 872*m*, 858*s*, 791*m*, 776*s*, 734*m*, 696*m*, 680*m*, 642*m*, 611*m*. ^{1}H-NMR (300 MHz, $CDCl_3$; assignments based on DQFCOSY, HSQC, and HMBC spectra): 7.85 (*td*, $J = 11.7$, 1.2, H–C(2′)); 7.64 (*d*, $J = 16.2$, H–C(7′)); 7.59 (*dd*, $J = 7.8$, 3.9, H–C(3) and H–C(5) of Ph); 7.45–7.39 (*m*, H–C(2), H–C(4) and H–C(6) of Ph); 6.90 (*td*, $J = 11.7$, 1.2, H–C(3′)); 6.87 (*d*, $J = 16.2$, H–C(6′)); 6.65 (*dq*, $J = 11.7$, 1.2, H–C(1′)); 6.56 (*dt*, $J = 11.4$, 1.2, H–C(4′)); 5.75 (*d*, $J = 0.9$, H–C(5)); 5.41 (*s*, CH_2–N(3)); 5.19 (*s*, CH_2–N(1)); 3.48 (*s*, *Me*OCH_2–N(3)); 3.45 (*s*, *Me*OCH_2–N(1)). ^{13}C-NMR (75 MHz, $CDCl_3$; assignments based on a HSQC and HMBC spectrum): 189.76 (*s*, C(5′)); 161.66 (*s*, C(4)); 152.30 (*s*, C(2)); 148.75 (*s*, C(6)); 144.10 (*d*, C(7′)); 135.36 (*d*, C(3′)); 134.21 (*s*, C(1) of Ph); 133.74 (*d*, C(2′)); 130.74 (*d*, C(4) of Ph); 129.26 (*d*, C(4′)); 128.89 (*d*, C(3) and C(5) of Ph); 128.37 (*d*, C(2) and C(6) of Ph); 127.04 (*d*, C(6′)); 126.18 (*d*, C(1′)); 104.63 (*d*, C(5)); 75.86 (*t*, CH_2–N(1)); 72.22 (*t*, CH_2–N(3)); 57.99 (*q*, *Me*OCH_2–N(3)); 57.22 (*q*, *Me*OCH_2–N(1)). HR-MALDI-MS: 421.1160 (18, $[M + K]^+$, $C_{21}H_{22}KN_2O_5^+$; calc. 421.1166), 405.1418 (100, $[M + Na]^+$, $C_{21}H_{22}N_2NaO_5^+$; calc. 405.1426), 383.1598 (70, $[M + H]^+$, $C_{21}H_{23}N_2O_5^+$; calc. 383.1607).

*1,3-Bis(methoxymethyl)-6-[(1*E*,3*E*,6*E*)-5-oxo-7-phenylhepta-1,3,6-trien-1-yl]uracil* ((*E*,*E*,*E*)-**21**). A soln. of a mixture (*Z*,*Z*,*E*)-**21**/(*Z*,*E*,*E*)-**21**/(*E*,*E*,*E*)-**21**/(*E*,*Z*,*E*)-**21** (1.6 g, 4.19 mmol) in MeOH (30 ml) was stirred at r.t. for 7 d when TLC (AcOEt/cyclohexane 3 : 1) evidenced the complete disappearance of (*Z*,*Z*,*E*)-**21**. Evaporation and crystallization from cyclohexane/AcOEt 5 : 1 gave (*E*,*E*,*E*)-**21** (1.10 g, 60%). Yellow solid. M.p. 170.0–170.4°. R_f (AcOEt/cyclohexane 3 : 1) 0.68. UV: 202 (4.41), 340 (4.47). IR (ATR): 3086*w*, 2982*w*, 2826*w*, 1704*m*, 1660*s*, 1645*s*, 1620*s*, 1575*s*, 1495*w*, 1433*s*, 1390*m*, 1361*m*, 1343*m*, 1320*m*, 1268*m*, 1254*m*, 1191*m*, 1172*m*, 1143*m*, 1093*s*, 1072*s*, 1021*m*, 1001*s*, 967*m*, 909*s*, 885*m*, 870*m*, 864*m*, 848*m*, 777*m*, 749*m*, 679*m*, 667*m*, 642*m*, 612*m*. ^{1}H-NMR (300 MHz, $CDCl_3$; assignments based on a DQFCOSY, a HSQC and a HMBC spectrum): 7.72 (*d*, $J = 15.9$, H–C(7′)); 7.61 (*dd*, $J = 6.6$, 3.6, H–C(2) and H–C(6) of Ph); 7.48–7.38 (*m*, H–C(3), H–C(4) and H–C(5) of Ph, H–C(3′)); 7.06–6.93 (*m*, H–C(1′), H–C(2′)); 6.99 (*d*, $J = 15.9$, H–C(6′)); 6.78 (*d*, $J = 15.3$, H–C(4′)); 6.01 (br. *s*, H–C(5)); 5.40 (*s*, CH_2–N(3)); 5.28 (*s*, CH_2–N(1)); 3.48 (*s*, *Me*OCH_2–N(1)); 3.46 (*s*, *Me*OCH_2–N(3)). ^{13}C-NMR

(75 MHz, $CDCl_3$): 188.26 (*s*, C(5′)); 162.07 (*s*, C(4)); 152.46 (*s*, C(2)); 150.79 (*s*, C(6)); 144.31 (*d*, C(7′)); 139.83 (*d*, C(3′)); 136.30 (*d*, C(2′)); 134.40 (*s*, C(1) of Ph); 133.20 (*d*, C(4′)); 130.87 (*d*, C(4) of Ph); 129.30 (*d*, C(1′)); 129.02 (*d*, C(2) and C(6) of Ph); 128.49 (*d*, C(3) and C(5) of Ph); 125.09 (*d*, C(6′)); 100.24 (*d*, C(5)); 75.71 (*t*, CH_2–N(1)); 72.24 (*t*, CH_2–N(3)); 57.91 (*q*, *Me*OCH_2–N(3)); 57.12 (*q*, *Me*OCH_2–N(1)). HR-MALDI-MS: 421.1160 (26, $[M + K]^+$, $C_{21}H_{22}KN_2O_5^+$; calc. 421.1166), 405.1425 (81, $[M + Na]^+$, $C_{21}H_{22}N_2NaO_5^+$; calc. 405.1426), 383.1599 (100, $[M + H]^+$, $C_{21}H_{23}N_2O_5^+$; calc. 383.1607). Anal. calc. for $C_{21}H_{22}N_2O_{.5}$ (382.42): C 65.96, H 5.80, N 7.33; found: C 65.67, H 5.88, N 7.28.

REFERENCES

[1] A. Ritter, D. Egli, B. Bernet, A. Vasella, *Helv. Chim. Acta* **2008**, *91*, 673.
[2] A. Vasella, *Chimia* **2005**, *59*, 785.
[3] W. Pfleiderer, K.-H. Schündehütte, *Liebigs Ann. Chem.* **1958**, *612*, 158; G. Strauss, *Liebigs Ann. Chem.* **1960**, *638*, 205; V. J. Ram, W. R. Knappe, W. Pfleiderer, *Liebigs Ann. Chem.* **1982**, 762.
[4] N. Boudet, P. Knochel, *Org. Lett.* **2006**, *8*, 3737; T. Nagamatsu, T. Fujita, K. Endo, *J. Chem. Soc., Perkin Trans. 1* **2000**, 33; H. Tanaka, H. Takashima, M. Ubasawa, K. Sekiya, N. Inouye, M. Baba, S. Shigeta, R. T. Walker, E. De Clercq, T. Miyasaka, *J. Med. Chem.* **1995**, *38*, 2860; H. Wamhoff, J. Dzenis, K. Hirota, *Adv. Heterocycl. Chem.* **1992**, *55*, 129.
[5] H. P. M. Thiellier, G. J. Koomen, U. K. Pandit, *Tetrahedron* **1977**, *33*, 1493; H. P. M. Thiellier, A. M. van den Burg, G.-J. Kooman, U. K. Pandit, *Heterocycles* **1974**, *2*, 467.
[6] P. F. Torrence, B. Witkop, *Biochemistry* **1972**, *11*, 1737; T. Kunieda, B. Witkop, *J. Am. Chem. Soc.* **1971**, *93*, 3478; T. Kunieda, B. Witkop, *J. Am. Chem. Soc.* **1969**, *91*, 7751.
[7] I. M. Lagoja, *Chem. Biodivers.* **2005**, *2*, 1.
[8] K. S. Jain, T. S. Chitre, P. B. Miniyar, M. K. Kathiravan, V. S. Bendre, V. S. Veer, S. R. Shahane, C. J. Shishoo, *Curr. Sci.* **2006**, *90*, 793; L. A. Agrofoglio, *Curr. Org. Chem.* **2006**, *10*, 333.
[9] R. Schaumann, 'Houben-Weyl: Hetarenes IV (Six- and Higher-membered Ring Systems With Two or more Heteroatoms)', Thieme Interscience, 1996.
[10] D. J. Brown, R. F. Evans, W. B. Cowden, M. D. E. Fenn, 'The Pyrimidine', Wiley-Interscience, New York, 1994.
[11] P. Norris, H. Shechter, *J. Org. Chem.* **1999**, *64*, 7290.
[12] V. Dave, E. W. Warnhoff, *Org. React.* **1970**, *18*, 217; S. D. Burke, P. A. Grieco, *Org. React.* **1979**, *26*, 361.
[13] J. Adams, D. M. Spero, *Tetrahedron* **1991**, *47*, 1765; T. Ye, M. A. McKervey, *Chem. Rev.* **1994**, *94*, 1091; I. Ojima, M. Tzamarioudaki, Z. Li, R. J. Donovan, *Chem. Rev.* **1996**, *96*, 635; M. P. Doyle, M. N. Protopopova, *Tetrahedron* **1998**, *54*, 7919; G. H. P. Roos, C. E. Raab, *S. Afr. J. Chem.* **2001**, *54*, 7; C. A. Merlic, A. L. Zechman, *Synthesis* **2003**, 1137.
[14] A. Padwa, K. E. Krumpe, *Tetrahedron* **1992**, *48*, 5385; A. Padwa, *J. Organomet. Chem.* **2001**, *617*, 3.
[15] V. F. Ferreira, L. O. R. Pereira, M. C. B. V. de Souza, A. C. Cunha, *Quim. Nova* **2001**, *24*, 540; V. F. Ferreira, *Curr. Org. Chem.* **2007**, *11*, 177.
[16] G. Maas, *Chem. Soc. Rev.* **2004**, *33*, 183.
[17] H. M. L. Davies, Ø. Loe, *Synthesis* **2004**, 2595; H. M. L. Davies, R. E. J. Beckwith, *Chem. Rev.* **2003**, *103*, 2861.
[18] P. M. P. Gois, C. A. M. Afonso, *Eur. J. Org. Chem.* **2004**, 3773; P. Bulugahapitiya, Y. Landais, L. Parra-Rapado, D. Planchenault, V. Weber, *J. Org. Chem.* **1997**, *62*, 1630; D. J. Miller, C. J. Moody, *Tetrahedron* **1995**, *51*, 10811; M. P. Doyle, *Adv. Chem. Ser.* **1992**, 443.
[19] G. Mehta, S. Muthusamy, *Tetrahedron* **2002**, *58*, 9477.
[20] C. Chatgilialoglu, C. Ferreri, M. Guerra, V. Timokhin, G. Froudakis, T. Gimisis, *J. Am. Chem. Soc.* **2002**, *124*, 10765.
[21] T.-L. Su, J.-T. Huang, J. H. Burchenal, K. A. Watanabe, J. J. Fox, *J. Med. Chem.* **1986**, *29*, 709.
[22] E. Pretsch, T. Clerc, J. Seibl, W. Simon, 'Tabellen zur Strukturaufklärung organischer Verbindungen mit spektroskopischen Daten', Springer-Verlag, Berlin, 1990, p. H175.
[23] G. L'abbé, F. Godts, S. Toppet, *J. Chem. Soc., Chem. Commun.* **1985**, 589; D. Moderhack, K.-H. Goos, *Chem. Ber./Recl.* **1987**, *120*, 921; J. Wang, G. Burdzinski, T. L. Gustafson, M. S. Platz, *J. Org. Chem.* **2006**, *71*, 6221.

[24] D. W. Adamson, J. Kenner, *J. Chem. Soc.* **1935**, 286; C. D. Hurd, S. C. Lui, *J. Am. Chem. Soc.* **1935**, *57*, 2656; J. Marx, L. Marx-Moll, *Chem. Ber.* **1954**, *87*, 1499; J. L. Brewbaker, H. Hart, *J. Am. Chem. Soc.* **1969**, *91*, 711; R. J. Bailey, P. J. Card, H. Shechter, *J. Am. Chem. Soc.* **1983**, *105*, 6096; K. Ito, J. Maruyama, *J. Heterocycl. Chem.* **1988**, *25*, 1681.

[25] G. W. Kirby, W. Lösel, P. S. Rao, D. J. Robins, M. A. Sefton, R. R. Talekar, *J. Chem. Soc., Chem. Commun.* **1983**, 810; R. G. S. Berlinck, R. Britton, E. Piers, L. Lim, M. Roberge, R. M. da Rocha, R. J. Andersen, *J. Org. Chem.* **1998**, *63*, 9850; P. H. Bernardo, C. L. L. Chai, *J. Org. Chem.* **2003**, *68*, 8906; M. Li, A. Wu, P. Zhou, *Tetrahedron Lett.* **2006**, *47*, 3707.

[26] R. Behrend, *Liebigs Ann. Chem.* **1888**, *245*, 213; F. L. Rose, *J. Chem. Soc.* **1952**, 3448; R. K. Robins, F. W. Furcht, A. D. Grauer, J. W. Jones, *J. Am. Chem. Soc.* **1956**, *78*, 2418; V. Papesch, R. M. Dodson, *J. Org. Chem.* **1963**, *28*, 1329.

[27] C. O. Kappe, G. Färber, *J. Chem. Soc., Perkin Trans. 1* **1991**, 1342; R. Saladino, L. Stasi, C. Crestini, R. Nicoletti, M. Botta, *Tetrahedron* **1997**, *53*, 7045; G. L'abbé, M.-A. Persoons, S. Toppet, *Magn. Reson. Chem.* **1987**, *25*, 362; P. Franchetti, L. Messini, L. Cappellacci, M. Grifantini, A. Lucacchini, C. Martini, G. Senatore, *J. Med. Chem.* **1994**, *37*, 2970.

[28] L. Bauer, D. Dhawan, C. S. Mahajanshetti, *J. Org. Chem.* **1966**, *31*, 2491.

[29] O. Temme, S.-A. Taj, P. G. Andersson, *J. Org. Chem.* **1998**, *63*, 6007.

[30] A. J. Anciaux, A. J. Hubert, A. F. Noels, N. Petiniot, P. Teyssié, *J. Org. Chem.* **1980**, *45*, 695; M. P. Doyle, W. H. Tamblyn, W. E. Buhro, R. L. Dorow, *Tetrahedron Lett.* **1981**, *22*, 1783; M. P. Doyle, V. Bagheri, T. J. Wandless, N. K. Harn, D. A. Brinker, C. T. Eagle, K.-L. Loh, *J. Am. Chem. Soc.* **1990**, *112*, 1906; A. Jeganathan, S. K. Richardson, R. S. Mani, B. E. Haley, D. S. Watt, *J. Org. Chem.* **1986**, *51*, 5362; A. de Meijere, T.-J. Schulz, R. R. Kostikov, F. Graupner, T. Murr, T. Bielfeldt, *Synthesis* **1991**, 547; P. Müller, C. Baud, D. Ené, S. Motallebi, M. P. Doyle, B. D. Brandes, A. B. Dyatkin, M. M. See, *Helv. Chim. Acta* **1995**, *78*, 459.

[31] E. Wenkert, M. Guo, R. Lavilla, B. Porter, K. Ramachandran, J.-H. Sheu, *J. Org. Chem.* **1990**, *55*, 6203.

[32] S. A. Matlin, L. Chan, B. Catherwood, *J. Chem. Soc., Perkin Trans. 1* **1990**, 89.

[33] J. A. Monn, M. J. Valli, S. M. Massey, M. M. Hansen, T. J. Kress, J. P. Wepsiec, A. R. Harkness, J. L. Grutsch, R. A. Wright, B. G. Johnson, S. L. Andis, A. Kingston, R. Tomlinson, R. Lewis, K. R. Griffey, J. P. Tizzano, D. D. Schoepp, *J. Med. Chem.* **1999**, *42*, 1027.

[34] E. V. Blackburn, C. J. Timmons, *Q. Rev. Chem. Soc.* **1969**, *23*, 482; D. Bryce-Smith, A. Gilbert, *MTP Int. Rev. Sci.: Org. Chem., Ser. 1* **1973**, *3*, 105.

[35] H. Laatsch, H. Beck, E. Egert, *Liebigs Ann. Chem.* **1992**, 1125.

[36] J.-R. Cui, Y.-J. Jian, Y.-K. Wu, S.-M. Wang, *Chin. J. Chem.* **2006**, *24*, 1163; C. Bruntner, T. Binder, W. Pathom-aree, M. Goodfellow, A. T. Bull, O. Potterat, C. Puder, S. Hörer, A. Schmid, W. Bolek, K. Wagner, G. Mihm, H.-P. Fiedler, *J. Antibiot.* **2005**, *58*, 346; G. B. Caygill, D. S. Larsen, S. Brooker, *J. Org. Chem.* **2001**, *66*, 7427; U. Flörke (University of Paderborn), private communication to Cambridge Database, 2000; T. Rozek, E. R. T. Tiekink, D. K. Taylor, J. H. Bowie, *Aust. J. Chem.* **1998**, *51*, 1057; A. M. Hassan, M. C. Cone, C. R. Melville, S. J. Gould, *Bioorg. Med. Chem. Lett.* **1995**, *5*, 191.

[37] J. Novák, J. Ratuský, V. Šneberk, F. Šorm, *Collect. Czech. Chem. Commun.* **1957**, *22*, 1836; L. Canonica, E. Fedeli, A. Castelnuovo, *Gazz. Chim. Ital.* **1957**, *87*, 998; B. Martín-Vaca, H. Rudler, M. Audouin, M. Nicolas, T. Durand-Réville, B. Vissière, *J. Organomet. Chem.* **1998**, *567*, 119; F. Löffler, M. Hagen, U. Lüning, *Synlett* **1999**, 1826.

[38] R. Paul, S. Tchelitcheff, *C. R. Hebd. Seances Acad. Sci.* **1957**, *244*, 2806.

[39] T. Werle, L. Schäffler, G. Maas, *J. Organomet. Chem.* **2005**, *690*, 5562; G. Maas, T. Werle, M. Alt, D. Mayer, *Tetrahedron* **1993**, *49*, 881.

[40] G. O. Schenck, R. Steinmetz, *Liebigs Ann. Chem.* **1963**, *668*, 19.

[41] A. Caballero, M. M. Díaz-Requejo, S. Trofimenko, T. R. Belderrain, P. J. Pérez, *J. Org. Chem.* **2005**, *70*, 6101.

[42] O. M. Nefedov, V. M. Shostakovskii, M. Y. Samoilova, M. I. Kravchenko, *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1972**, *21*, 2281; C. Böhm, M. Schinnerl, C. Bubert, M. Zabel, T. Labahn, E. Parisini, O. Reiser, *Eur. J. Org. Chem.* **2000**, 2955.

[43] F.-G. Klärner, D. Schröer, *Chem. Ber.* **1989**, *122*, 179; F.-G. Klärner, D. Schröer, *Angew. Chem., Int. Ed.* **1987**, *26*, 1294.
[44] W. Steinkopf, H. Augestad-Jensen, *Liebigs Ann. Chem.* **1922**, *428*, 154.
[45] C. D. Bedford, P. A. S. Smith, *J. Org. Chem.* **1983**, *48*, 4002; R. J. Gillespie, A. E. A. Porter, *J. Chem. Soc., Perkin Trans. 1* **1979**, 2624.
[46] H.-U. Reissig, R. Zimmer, *Chem. Rev.* **2003**, *103*, 1151.
[47] J. E. Baldwin, *Chem. Rev.* **2003**, *103*, 1197.
[48] H. N. C. Wong, M.-Y. Hon, C.-W. Tse, Y.-C. Yip, J. Tanko, T. Hudlicky, *Chem. Rev.* **1989**, *89*, 165.
[49] H. M. L. Davies, N. Kong, M. R. Churchill, *J. Org. Chem.* **1998**, *63*, 6586.
[50] I. Reichelt, H.-U. Reissig, *Chem. Ber. Recl.* **1983**, *116*, 3895.
[51] V. M. S. Gil, W. von Philipsborn, *Magn. Reson. Chem.* **1989**, *27*, 409.

Received March 18, 2008