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Synthesis of 1,5-Dihydro-5-(4-methoxyphenyl)-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-ones and Their Ribosides and Mannich Bases

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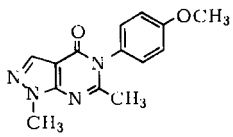
1,5-Dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-ones **5** and **6** were prepared by reaction of the corresponding ethyl 5-aminopyrazole-4-carboxylate with triethyl orthoformate and amines. Ethyl *N*-(4-methoxyphenyl)formimidate and *N,N'*-bis(4-methoxyphenyl)formamidine could also be used as the ring closing reagent. The *Mannich* bases **13** and **14** were produced in a reaction of **9** with formaldehyde and piperidine. The ribosides **15** were obtained by melting a mixture of **9** and 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose in the presence of *p*-toluenesulphonic acid.

Synthese von 1,5-Dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-onen und ihrer Riboside und Mannichbasen

Bei der Umsetzung von 5-Aminopyrazol-4-carbonsäure-ethylester **(2)** mit Orthoameisensäure-triethylester und Aminen wurden die 1,5-Dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one **5** und **6** erhalten. Auch N-(4-Methoxyphenyl)-formimidsäure-ethylester und N,N'-Bis(4-methoxyphenyl)-formamidin konnten als Ringschlußreagenzien verwendet werden. **9** wurde mit Formaldehyd und Piperidin in die *Mannich* Basen **13** und **14** überführt. Schmelzen von **9** und 1,2,3,5-Tetra-O-acetyl-β-D-ribofuranose mit einer katalytischen Menge Toluol-4-sulfonsäure lieferte die Riboside **15.**

In a previous work it was found that the pyrazolopyrimidinone **1** was active against lymphocytic leukemia in mice[1].



1

The 4-methoxy group in the phenyl ring was a condition of the anti-cancer activity. Replacement of 6-CH_3 with other alkyl groups resulted in inactive compounds.

The aim of the present work was to improve the anticancer activity by replacing 1-CH_3 either with an aminomethyl or with a ribosyl group. It was also our intention to investigate the change in activity if no substituent was present in the 6-position of the pyrazolopyrimidinone.

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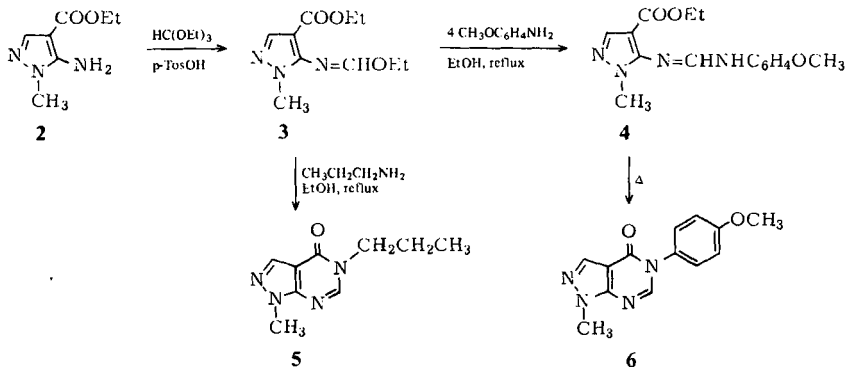
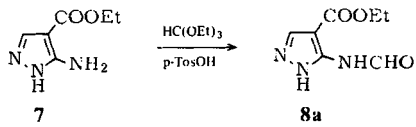


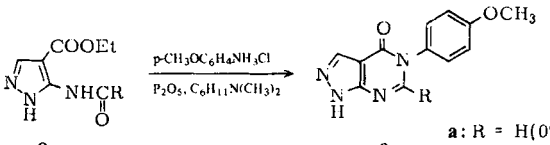
The ethoxymethylene derivative **3** was obtained in 76 % yield by refluxing the aminopyrazole **2** in triethyl orthoformate in the presence of a catalytic amound of p-toluenesulphonic acid. **3** was a rather labile compound which decomposed into **2** on standing. This was a hindrance to obtaining correct microanalysis of **3** although ^{1}H-NMR showed that freshly prepared compound was absolutely pure containing no traces of **2**.

It was also attempted to prepare **3** from **2** using $CH_3COOCH(OEt)_2$ as the ethoxymethylenation reagent which has been used succesfully by *Taylor* and *Hartke* for introducing the ethoxymethylene group into 5-amino-4-pyrazolecarbonitriles[2]. However, this procedure resulted in low yields of **3** mixed with ethyl 5-acetylamino-1-methyl-1*H*-pyrazole-4-carboxylate.

The ethoxymethylene derivative **3** was reacted with p-anisidine in refluxing anhydrous ethanol to give **4** which was cyclized to the pyrazolopyrimidinone **6** by heating in vacuum above its melting point. Reaction of **3** with propylamine resulted in formation of the ring closed product **5**. In this case an intermediate corresponding to **4** is likely because TLC showed the presence of an intermediate compound during the reaction. The synthesis of **5** and **6** nicely demonstrates the importance of the nucleophilicity of the ring closing nitrogen atom in the ring closure reaction.

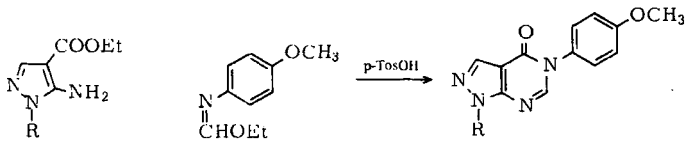


The attempt to use the aminopyrazolecarboxylate **7** in a similar way instead of **2** as starting material was unsuccesful. It was not possible to obtain the intermediate product corresponding to **3**. Instead, reaction of **7** with excess of triethyl orthoformate resulted in the formylaminopyrazolecarboxylate **8a** in 93 % yield. Reaction of **7** according to the procedure of *Taylor* and *Hartke*[2] with $CH_3COOH(OEt)_2$ resulted in a mixture of **8a** and ethyl 5-acetylamino-1*H*-pyrazole-4-carboxylate.



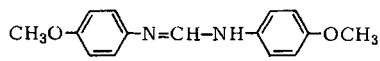
8 **9** **a**: R = H(0%) **b**: R = CH_3(48%)

By analogy with our earlier observations[3] we believed that it was possible to prepare the N-1 unsubstituted pyrazolopyrimidinone **9a** by heating the ready available formylamino derivative **8a** with a mixture of phosphorus pentoxide, p-anisidine hydrochloride and N,N-dimethylcyclohexylamine. However, we failed to isolate any ring closed product **9a** in this way. Nevertheless, it was possible to prepare the corresponding 6-methyl substituted compound **9b** by reacting the acetylamino derivative **8b** with the same reagent mixture.



10 **11** **6** R = CH_3 **9a** R = H

Failing to prepare the N-1 unsubstituted formamidine intermediate in the same way as for **4** in the synthesis of the pyrazolopyrimidinone **9a**, we instead refluxed the aminopyrazole **10** with ethyl N-(4-methoxyphenyl)formimidate **11** in the presence of a catalytic amount of p-toluenesulphonic acid in xylene and **9a** was obtained in 69 % yield. Lower boiling solvents such as ethanol or butanol could not be used. The reaction could also take place without any solvent by heating at 200°C for 20 min at reduced pressure, but only 30 % yield was obtained. The N-1 methyl substituted pyrazolopyrimidinone **6** could be prepared, similarly, using xylene as solvent. **9a** was also obtained in 47 % yield by using the amidine **12** instead of **11.**

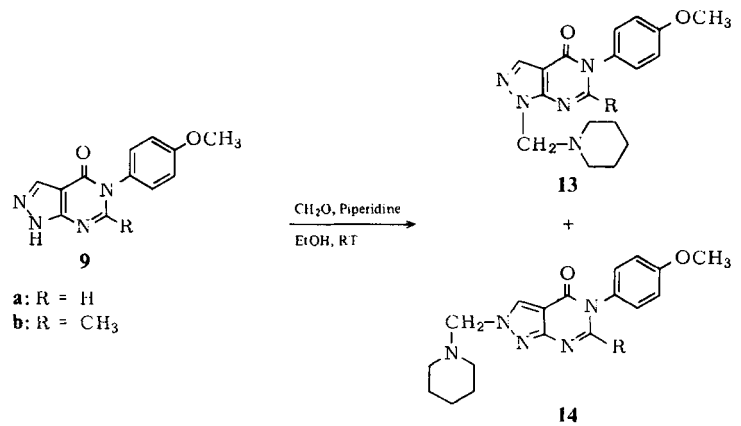


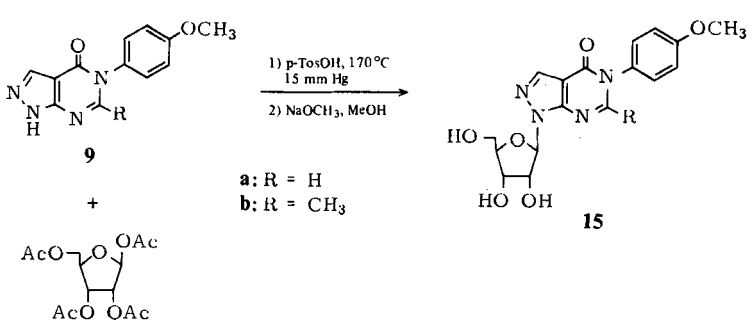
12

11 was smoothly prepared from p-anisidine and excess of triethyl orthoformate in 80 % yield using catalytic amounts of p-toluenesulphonic acid. A similar reaction with trimethyl orthoformate produced the amidine **12** in high yield.

Mannich bases of allopurinol have been suggested as prodrugs in gout therapy. The idea is that allopurinol can be made more easily available for biologically systems if it is transformed into its *Mannich* base derivative which then, after the taking up in the body can be regenerated by hydrolysis[4]. By reaction of **9** with formaldehyde and piperidine we

were also able to prepare the corresponding *Mannich* bases. In analogy to our previous *Mannich* base syntheses from N-5 substituted pyrazolopyrimidinones[3], but in contrast to the observations of *Bundgaard* and *Johansen*[4] for allopurinol, we observed a reaction at both N-1 and N-2 of **9** and we isolated a mixture of the *Mannich* bases **13** and **14** in the ration 3 : 1.





The ribosides **15** were prepared from **9** in a fusion reaction with 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose. Since **9** were high melting compounds it was attempted to prepare their trimethylsilyl derivatives to be used in the fusion reaction according to known procedures[5,6]. The yields may sometimes be improved because a lower reaction temperature can be used for the lower melting trimethylsilyl derivatives. However, we did not succeed in obtaining the silyl derivatives of **9** by reaction with hexamethyldisilazane in presence of the usual catalyst, such as trimethylsilyl chloride, ammonium sulphate or pyridine.

6, 9a, 13a and **13b** were tested against P 388 lymphocytic leukemia whereas **15a** and **15b** were tested against L-1210 lymphoid leukemia, but no activity was observed[11].

Experimental Part

Ethyl 5-ethoxymethylenimino-1-methyl-1H-pyrazole-4-carboxylate **(3)**

11.0 g (65 mmol) ethyl 5-amino-1-methyl-1*H*-pyrazole-4-carboxylate[7], 0.30 g (1.7 mmol) p-toluenesulphonic acid and 60 g (0.4 mol) triethyl orthoformate were refluxed for 40 min. Excess of triethyl orthoformate was distilled off under reduced pressure and the remaining oil was taken up in hot pentane and filtered. Precipitation was provoked by a dry ice acetone cooling bath and the product was filtered off below -10°C. The mother liquid was concentrated and filtration was repeated. Yield 11.2 (76 %) of **3**, m.p. 40.5–43°C. ^{1}H-NMR (DMSO-d_6): δ (ppm) = 8.35 (s, 1H, OCH=), 7.80 (s, 1H, 3-H), 3.9–4.6 (m, 4H, 2×OCH_2), 3.62 (s, 3H, NCH_3), 1.1–1.4 (m, 6H, 2×CH_3); ^{13}C-NMR (DMSO-d_6): δ (ppm) = 162.48 (O–CH=), 148.16 (–COO–), 140.01 (C-3), 101.11 (C-4), 62.93 (CH–O–CH_2), 59.23 (O–CH_2), 34.61 (N–CH_3), 14.12 (CH_3) 13.93 (CH_3).

Ethyl 5-(4-methoxyanilino)-methylenimino-1-methyl-1H-pyrazole-4-carboxylate **(4)**

4.0 g (18 mmol) **3**, 3.0 g (24 mmol) p-anisidine and 50 ml absol. ethanol were refluxed for 14 h. **4** precipitated on cooling and was isolated by filtration. Yield 2.42 g (45 %) of **4**, m.p. 165–166°C (absol. EtOH). ^{1}H-NMR (CF_3COOD): δ (ppm) = 8.91 (s, 1H, NH–CH), 7.90 (s, 1H, NH)), 7.81 (s, 1H, 3-H), 6.92 (m, 4H, ArH), 4.24 (q, J = 7.2Hz, 2H, CH_2), 3.79 (s, 3H, CH_3), 3.70 (s, 3H, CH_3), 1.31 (t, J = 7.2 Hz, 3H, CH_3); $C_{15}H_{18}N_4O_3$ Calcd. C 59.6 H 6.00 N 18.5; Found: C 59.4 H 5.98 N 18.6.

1,5-Dihydro-1-methyl-5-propyl-4H-pyrazolo [3,4-d] pyrimidin-4- one **(5)**

3.0 g (13 mmol) **3**, 2.1 g (36 mmol) propylamine and 100 ml absol. ethanol were refluxed for 3 h. Evaporation at reduced pressure afforded an oil from which **5** was precipitated by addition of 80 ml diethyl ether. Yield 0.90 g (35 %) of **5**, m.p. 119.5–120.0 °C (toluene/ligroin, b.p. 80–100 °C). ^{1}H-NMR (DMSO-d_6): δ(ppm) = 8.42 (s, 1H, 6-H), 8.06 (s, 1H, 3-H), 3.96 (t, 2H, N-CH_2), 3.93 (s, 3H, N-CH_3), 1.4–2.0 (m, 2H, CH_2), 0.90 (t, 3H, CH_3); ^{13}C-NMR (DMSO-d_6) = δ(ppm) = 156.38 (C-4), 151.21 (C-7a), 150.47 (C-6), 134.00 (C-3), 104.94 (C-3a), 46.85 (N-CH_2), 33.87 (N-CH_3), 22.37 (CH_2) 10.72 (CH_3); $C_9H_{12}N_4O$ Calcd. C 56.2 H 6.29 N 29.2: Found: C 56.6 H 6.36 N 29.2.

1,5-Dihydro-5-(4-methoxyphenyl)-1-methyl-4H-pyrazolo[3,4-d]pyrimidin-4-one **(6)**

Method A: 2.0 g (6 mmol) **4** were heated at 150 °C/15 mmHg for 10 min and allowed to cool to room temp. The solidified material was crushed and recrystallized from toluene and then from methanol. Yield 1.27 g (75 %) of **6**,

Method B: 10.0 g (59 mmol) **2**[7] 20.0 g (112 mmol) **11**[9] and 0.60 g (3 mmol) p-toluenesulphonic acid in 250 ml xylene were refluxed for 24 h. **6** precipitated on cooling. From methanol 8.9 g (59 %) of **6**. M.p. 224.5–225.5 °C. ^{1}H-NMR (DMSO-d_6): δ(ppm) = 8.33 (s, 1H, 6-H), 8.13 (s, 1H, 3-H), 6.9–7.5 (4H, m, C_6H_4), 3.95 (s, 3H, N-CH_3), 3.82 (s, 3H, OCH_3). ^{13}C-NMR DMSO-d_6: δ(ppm) = 150.23 (C-6), 134.44 (C-3), 159.19 129.56 128.86 114.19 (C_4H_4), 104.84 (C-3a), 55.35 (OCH_3), 33.9 (N-CH_3); UV (EtOH): λmax (log ε) = 267 (3.9), 211 (4.5) nm; $C_{13}H_{12}N_4O$ Calcd. C 60.9 H 4.72 N 21.9; Found: C 60.7 H 4.67 N 21.8.

Ethyl 5-formylamino-1H-pyrazole-4-carboxylate **(8a)**

20.0 g **7**[3] and 140 ml triethyl orthoformate were refluxed for 4 h. Excess of triethyl orthoformate was distilled off under reduced pressure and the remaining crude oil was recrystallized from absol. ethanol to give 19.2 g (81 %) of **8a**. M.p. 191–193 °C, lit.[8] m.p. 192.5–193.5.

1,5-Dihydro-5-(4-methoxyphenyl)-4H-pyrazolo[3,4-d]pyrimidin-4-one **(9a)**

Method A: 10.0 g (65 mmol) **10**, 20.0 g (112 mmol) **11**[9] and 0.6 g (3 mmol) p-toluenesulphonic acid in 250 ml xylene were refluxed for 20 h. The reaction mixture was allowed to cool to room temp. and was extracted with 5 × 100 ml 2M-NaOH. The combined water phases were extracted with 2 × 100 ml ether. The combined water phases were then adjusted to pH 5 with conc. HCl. Filtration and recrystallization from methanol afforded 10.7 g (69 %) of **9a**.

Method B: 1.0 g (6.5 mmol) **10**, 5.0 g (20 mmol) **12**[10] and 50 mg (0.3 mmol) p-toluenesulphonic acid in 15 ml xylene were refluxed for 20 h. Work up as above yielded 0.6 g (40 %) of **9a**. M.p. 274–276 °C. ^{1}H-NMR (DMSO-d_6) = δ(ppm) = 8.24 (s, 2H, 3-H and 6-H), 6.9–7.5 (m, 4H, C_6H_4), 3.82 (s, 3H, CH_3); ^{13}C-NMR (DMSO-d_6): δ(ppm) = 157.05 (C-4), 154.00 (C-7a), 149.84 (C-6) 133.86 (C-3), 159.19 130.03 128.93 114.25 (C_6H_4), 104.90 (C-3a), 55,42 (CH_3); UV (EtOH): λmax (log ε) = 263 (3.8), 226 (4.2), 204 (4.5) nm; $C_{12}H_{10}N_4O_2$ Calcd. C 59.5 H 4.16 N 23.1; Found C 59.4 H 4.11 N 23.0.

1,5-Dihydro-5-(4-methoxyphenyl)-6-methyl-4H-pyrazolo[3,4-d]pyrimidin-4-one **(9b)**

36.4 g (0.26 mol) P_2O_5, 38.8 g (0.31 mol) N,N-dimethylcyclohexylamine and 24.4 g (0.13 mol) 4-methoxyaniline hydrochloride were mixed thoroughly by mechanical stirring in a 3-necked flask with condenser and drying tube. The flask was transferred to an oil bath preheated to 200 °C. A light brown glassy mixture was formed within a few min. The oil-bath was allowed to cool to 150 °C and 8.0 g (40 mmol) **8b**[3] were added. After heating for 140 min at 150 °C the reaction mixture was hydrolyzed by cautious addition of ice water. Keeping the temp. below 10 °C, 2M-NaOH was added until ph > 11. The organic phase was separated off, extracted with 2 × 50 ml 2M-NaOH and discarded. The alkaline water phases were combined and extracted with 3 × 50 ml CH_2Cl_2. The combined water phases were adjusted to pH 7 with conc. HCl and saturated $NaHCO_3$ keeping the temp. below 15 °C. After 20 min 5.9 g of **9b** were obtained by filtration. Additional 1.0 g of **9b** was obtained by extraction of the water phase with 3 × 100 ml $CHCl_3$. Recrystallization from absol. EtOH with decolorising carbon afforded 5.0 g 48 % of **9b**. M.p. 254.5–256.5 °C. ^{1}H-NMR (DMSO-d_6): δ(ppm) = 13.71 (s, 1H, NH), 8.13 (s, 1H, CH), 6.9–7.6 (m, 4H, C_6H_4), 3.84 (s, 3H, O-CH_3), 2.13 (s, 3H, CH_3); ^{13}C-NMR (DMSO-d_6): δ(ppm) = 157.94 (C-4 and C-6), 152.84 (C-7a), 135.08 (C-3), 159.17 130.34 129.62 114.59 (C_6H_4), 103.35 (C-3a), 55.33 (O-CH_3), 24.32 (6-CH_3); UV (EtOH): λmax (log ε) = 251 (3.9), 223 (4.2) nm; $C_{13}H_{12}N_4O_2$ Calcd. C 60.9 H 4.72 N 21.9; Found: C 60.7 H 4.72 N 21.7.

1,5-Dihydro-5-(4-methoxyphenyl)-1-piperidinylmethyl)-4H-pyrazolo[3,4-d]pyrimidin-4-one **(13a)** and *2,5-dihydro-5-(4-methoxyphenyl-2-(1-piperidinylmethyl)-4H-pyrazolo [3,4-d] pyrimidin-4-one* **(14a)**

2.0 g (8.3 mmol) **9a**, 1.44 g (17 mmol) piperidine and 17 ml absol. ethanol were stirred at room temp. for 1.5 h. 0.75 g (9.3 mmol) aqueous formaldehyde (37 %) was added and stirring at room temp. was continued for 90 h. The mixture was cooled to 5 °C and filtered. Yield 1.7 g (60 %) of a mixture of 70 % **13a** and 30 % **14a**. M.p. 154–156 °C (EtOH). ^{1}H-NMR (DMSO-d_6) of **13**: δ(ppm) = 8.43 (s, 1H, 6-H), 8.25 (s, 1H, 3-H), 6.7–7.7 (m, 4H, C_6H_4), 5.23 (s, 2H N-CH_2-N), 3.90 (s, 3H, CH_3), 2.31 (m, 4H, NCH_2), 1.47 (m, 6H $(CH_2)_3$). Typical ^{1}H-NMR peaks of **14a**: δ(ppm) = 8.33 (s, 6-H), 8.70 (s, 3-H); UV (EtOH): λmax (log ε) = 264 (3.9), 225 (sh), 206 (4.6) nm; $C_{18}H_{21}N_5O_2$ Calcd. C 63.7 H 6.24 N 20.6 Found: C 63.3 H 6.15 N 20.6.

1,5-Dihydro-5-(4-methoxyphenyl)-6-methyl-1-(1-piperidinylmethyl)-4H-pyrazolo[3,4d]pyrimidin-4-one **(13b)** and *2,5-dihydro-5-(4-methoxyphenyl)-6-methyl-2-(1-piperidinylmethyl)-4H-pyrazolo-[3,4-d]pyrimidin-4-one* **(14b)**

2.0 g (7.8 mmol) **9b**, 1.33 g (15.6 mmol) piperidine and 25 ml absol. ethanol were stirred 1 h at room temp. and 0.70 g (8.7 mmol) aqueous formaldehyde (37 %) was added. After stirring for 24 h at room temp. the mixture was cooled to 5 °C. Yield 2.5 g (91 %) of a mixture of 75 % **13b** and 25 % **14b**. M.p. 188–189 °C (EtOH). ^{1}H-NMR (DMSO-d_6): of **13b**: δ(ppm) = 8.07 (s, 1H, 3-H), 6.9–7.4 (m, 4H, C_6H_4), 5.10 (s, 2H, N-CH_2-N), 3.82 (s, 3H, OCH_3), 2.50 (m, 4H, NCH_2), 2.14 (s, 3H, CH_3), 1.38 (m, 6H, $(CH_2)_3$); Typical ^{1}H-NMR peaks of **14b** δ(ppm) =: 8.52 (s, 3-H) 2.07 (s, CH_3); UV (EtOH): λmax (log ε) = 252 (3.9), 223 (sh), 204 (4.6) nm; $C_{19}H_{23}N_5O_2$ Calc. C 64.6 H 6.56 N 19.8 Found: C 64.5 H 6.54 N 19.9.

1,5-Dihydro-5-(4-methoxyphenyl)-1-(β-D-ribofuranosyl)-4H-pyrazolo[3,4-d]pyrimidin-4-one **(15a)**

4.84 g (20 mmol) **9a**, 7.3 g (23 mmol) 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose were heated in an oil bath with mechanical stirring at 170 °C for 5 min. 0.3 g (1.5 mmol) p-toluenesulphonic acid was added and a vac. of 15 mmHg was quickly applied during the heating of the mixture at 170 °C for 25 min. The cooled reaction mixture was dissolved in 250 ml $CHCl_3$ and washed with 50 ml saturated $NaHCO_3$. The organic phase was dried over Na_2SO_4. $CHCl_3$ was destilled off leaving a black oil which was suspended in 300 ml MeOH and filtered. The filtrate was evaporated i. vac. and the remaining material was dissolved in 20 ml CH_2Cl_2 and subjected to preparative silica TLC with MeOH/CH_2Cl_2 (1:50) using 9 plates (3 × 250 × 300 mm silica layer) which were eluted 5 times (Recycling silica HPLC was unsuccessful in our hands). Extraction of the TLC bands with MeOH in the cold afforded 5.1 g (10.1 mmol) peracetylated **15a** which was dissolved in 50 ml MeOH and added to 600 ml (12 mmol) 0.02 M-NaOMe freshly prepared in anhydrous MeOH. The mixture was stirred 1 h at room temp. and **15a** was collected. From, H_2O/MeOH (1:2) 3.05 g (41 %) of **15a**. M.p. 237–239 °C. ^{1}H-NMR (DMSO-d_6): δ(ppm) = 8.39 (s, 1H, 6-H), 8.26 (s, 1H, 3-H), 7.0–7.6 (m, 4H, C_6H_4), 6.11 (d, 1H, J = 4.15 Hz, 1'-H), 3.82 (s, 3H, CH_3); ^{13}C-NMR (DMSO-d_6): δ(ppm) = 156.34 (C-4), 152.16 (C-7a), 150.99 (C-6), 135.92 (C-3), 159.30 129.87 128.90 114.23 (C_6H_4), 105.53 (C-3a), 88.25 (C-1'), 85.33 (C-4'), 73.32 (C-2'). 70.79 (C-3'), 62.21 (C-5'), 55.39 (OCH_3); UV (EtOH): λmax (log ε) = 269 (3.8), 210 (4.4) nm; MS: m/e (%) = 374 (M^+, 4), 285 (24), 271 (33), 255 (13), 244 (15), 243 (100), 242 (37), 134 (13), 110 (12); $C_{17}H_{18}N_4O_6$ Calcd. C 54.5 H 4.85 N 15.0 Found C 54.5 H 4.82 N 14.9.

1,5-Dihydro-5-(4-methoxyphenyl)-6-methyl-1-(β-D-ribofuranosyl)-4H-pyrazolo[3,4-d]pyrimidin-4-one **(15b)**

15b was prepared analogously to **15a**. Yield: 1.0 g (13 %) of **15b**. M.p. 231–232° (2-propanol); ^{1}H-NMR (DMSO-d_6): δ(ppm) = 8.17 (s, 1H, 3-H), 7.2–7.5 (m, 4H, C_6H_4), 6.10 (d, 1H, J = 4.63 Hz, 1'-H), 3.82 (s, 3H, OCH_3), 2.16 (s, 3H, 6-CH_3); ^{13}C-NMR (DMSO-d_6): δ(ppm) = 157.50 (C-4 and C-6), 151.59 (C-7a), 135.62 (C-3), 159.25 129.97 129.45 114.58 (C_6H_4), 104.06 (C-3a), 88.08 (C-1'), 85.29 (C-4'), 73.14 (C-2'), 70.81 (C-3'), 62.23 (C-5'), 55.29 (OCH_3), 24.37 (6-CH_3); UV (EtOH): λmax (log ε) = 266 (3.9), 255 (3.9), 223 (sh), 207 (sh) nm; MS: m/e (%) = 388 (M^+, 1), 299 (27), 285 (44), 269 (14), 258 (15), 257 (100), 256 (28), 241 (23), 148 (36), 77 (11); $C_{18}H_{20}N_4O_6$ Calcd. C 55.7 H 5.19 N 14.4; Found C 55.6 H 5.18 N 14.2.

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Ein einstufiges Verfahren zur Darstellung von γ-Yliden-α,β-butenoliden[+)]

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In einem Eintopfverfahren können durch Umsetzung von Aldehyden bzw. deren Acetalen mit 2,5-Dihydro-2,5-dimethoxy-furan in Gegenwart von Trimethylchlorsilan γ-Yliden-α,β-butenolide **3** dargestellt werden. Der Reaktionsmechanismus wird diskutiert.

A Single-Step Process for the Preparation of γ-Ylidene-α,β-butenolides

One-pot reactions of aldehydes or their acetales with 2,5-dihydro-2,5-dimethoxyfuran in the presence of trimethylchlorosilane lead to γ-ylidene-α,β-butenolides **3.** The mechanism of the reaction is discussed.

Lactone sind nicht nur als Synthese-Zwischenprodukte von größerer Bedeutung, sondern auch wegen ihrer vielfältigen Bioaktivitäten wertvolle Präparate vor allem für die Pharmaindustrie.

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