Alkylamination of Pteridines by Primary Alkylamines - Potassium Permanganate

H. Sladowska, A. van Veldhuizen and H. C. van der Plas*

Laboratory of Organic Chemistry, Agricultural University, De Dreijen 5, 6703 BC Wageningen, The Netherlands

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Reaction of 7-phenyl, 7-*p*-methoxyphenyl, 7-*t*-butyl- and 6,7-diphenylpteridine with ethylamine and *t*-butylamine in the presence of potassium permanganate leads to the introduction of the ethylamino or *t*-butylamino group at C-4 in the above-mentioned pteridines. In the reaction of ethylamine/potassium permanganate besides the 4-(ethylamino)pteridine derivatives 2-amino-3-formylpyrazines are obtained as side-products. In the reaction with *t*-butylamine/potassium permanganate the corresponding pteridin-4-ones are obtained as by-products. The ^{1}H nmr spectroscopic studies have revealed that at room temperature ethylamine easily gives a σ-adduct at C-4, yielding a 4-(ethylamino)-3,4-dihydropteridine derivative. *t*-Butylamine, however, only gives with the pteridines addition at C-4 at low temperature, *i.e.* at -40°. This adduct dissociates at room temperature. *n*-Propylamine and *n*-butylamine show the same behavior as ethylamine.

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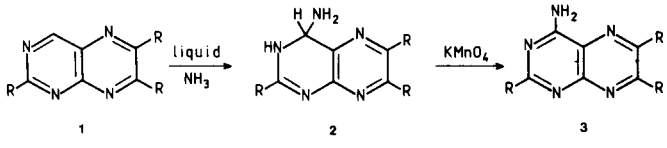
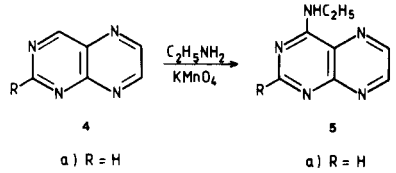
In an earlier paper [1] we reported that treatment of a solution of 7R-, 6,7-diR- and 2R-pteridines (**1**, R = alkyl or aryl) in liquid ammonia with potassium permanganate at +20° as well as at -40° gave a series of 4-amino-7-R-, 4-amino-6,7-diR- and 4-amino-2-R-pteridines **3** in good yields. ^{1}H nmr data convincingly show that in this amination reaction the 1:1 σ-adducts **2** are the actual species which undergo the oxidation.





Scheme 1

Some years ago it was found [2] that by using ethylamine instead of ammonia, the pteridines **4a** and **4b** undergo ethylamination at position 4 of the pteridine ring yielding **5a** and **5b** respectively. It is of interest that in compound **5b**, containing the labile chloro atom at C-2, no replacement of the chloro atom took place. These earlier results [2] induced us to extend our amination work by investigating the alkylamination of 7-mono and 6,7-disubstituted pteridines **6a-d**, using as primary amines ethylamine and *t*-butylamine and as oxidant potassium permanganate. Our reactions were carried out at a temperature of about 15°-20°.

A. Reaction of **6a-c** with Ethylamine/Potassium Permanganate.

A. 1. Product Identification.

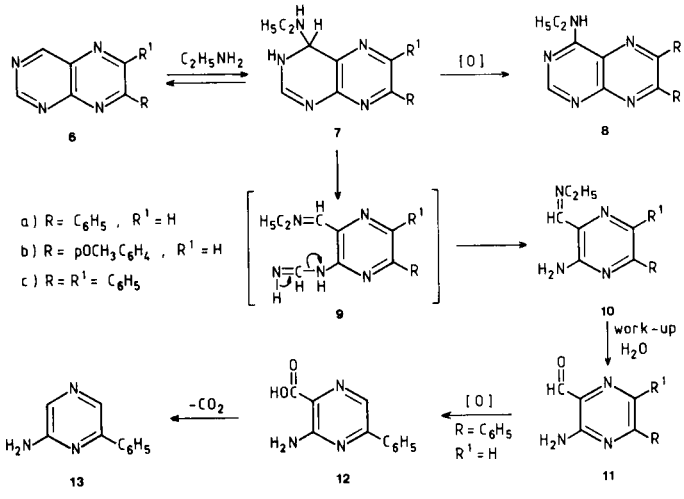
When the pteridines **6a-c** are reacted at 16°-17° with ethylamine in the presence of potassium permanganate, we found that after work-up of the reaction mixture the 4-(ethylamino)pteridines **8a-c** and in addition the 2-amino-3-formylpyrazines **11a-c** were formed. The yields of **8a-c** are rather low (**8a**, 26%; **8b**, 36%; **8c**, 14%) and the yields of the pyrazines **11a-c** amount to **11a**, 38%; **11b**, 18%; **11c**, 43%. The respective ir spectra of the pteridines **8a-c** showed the presence of only one NH-stretching frequency around 3200 cm^{-1}, characteristic for a secondary amino group.

Their ^{1}H nmr spectra exhibit one (**8c**) or two (**8a,b**) distinct low-field singlets (see Table 1), having almost the same chemical shifts as found in the 4-aminopteridines, synthesized previously [1]. These measurements provide ample evidence that the ethylamination of the pteridines **6a-c** leads to substitution at position 4 of the pteridine ring. The structure assignments of the unknown pyrazines **11a-c** were based on the following observations: the ir spectra showed two absorptions around 3400 cm^{-1} and 3270 cm^{-1}, the characteristic stretching frequencies of the aminogroup. Moreover a C=O absorption was found in the region 1670-1690 cm^{-1}. The ^{1}H nmr spectra of **11a-c** exhibit a very low field singlets (1H) around 10 ppm (**11a**, 10.5 ppm; **11b**, 10.0 ppm; **11c**, 10.1 ppm). They are ascribed to the presence of the formyl hydrogen. In case of the compounds **11a** and **11b** also the proton at C-5 (**11a**, 8.52 ppm; **11b**, 8.65 ppm) was clearly assigned.

The structure of one of the pyrazines, *i.e.* **11a**, was further confirmed by oxidative conversion of **11a** into the known compound 2-amino-3-carboxy-6-phenylpyrazine (**12**), which on decarboxylation gave 2-amino-6-phenylpy-

razine (**13**).

When **6a** was reacted with ethylamine at room temperature for a few hours without the presence of potassium permanganate the reaction took a different course. After evaporation of the ethylamine a yellow coloured product was isolated, which ^{1}H nmr spectrum features in the low field region one singlet (8.4 ppm) and triplet (8.5-8.44 ppm). Exact mass measurement showed that this compound has the molecular formula $C_{13}H_{14}N_4$. The ir spectrum features the presence of an aminogroup (3250, 3325 cm^{-1}) and a C=N group (1640 cm^{-1}). Based on this information and the microanalytical data we assigned to this product the structure of 2-amino-3-(ethyliminomethylene)-6-phenylpyrazine (**10a**).



Scheme 2

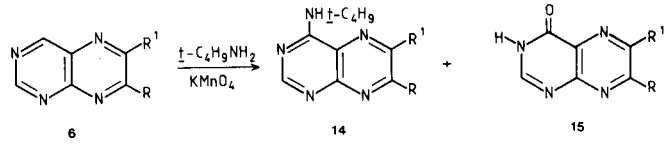
A. 2. Mechanism of the Reaction.

In order to establish whether these reactions described above would proceed *via* the intermediary 4-(ethylamino)-3,4-dihydropteridines **7** we measured the ^{1}H nmr spectra of a solution of **6a-c** in ethylamine at room temperature . As is shown in Table 1 it is evident that in this solution the absorption of H-4 is highly upfield shifted (~4 ppm), compared to the one found for H-4 in a solution of **6a-c** in deuteriochloroform. This upfield shift value is of the same magnitude as observed for the very unstable adduct formed between pteridine and ethylamine [2]. This upfield shift is caused by the formation of the σ-adducts **7a-c**, forcing C-4 to rehybridise from sp^2 to sp^3. Adducts **7a-c** are stable at room temperature but decompose on standing, in contrast to the adduct formed between pteridine and ethylamine, which decomposes rapidly even at -75° [2].

These measurements show that in these ethylamination reactions the initial product is the C-4 adduct **7a-c**. These adducts can undergo oxidation into **8a-c** in the presence of potassium permanganate or undergo ring fission between N-3 and C-4 yielding the pyrazine **9a-c** having as side chains the ethyliminomethylene group and the iminomethyleneamino group. A base-induced loss of hydrogen cyanide yields **10a-c**. The isolation of **10a** when potassium permanganate is absent strongly supports this mechanism. The formation of **11a-c**, actually isolated has occurred during work-up of the reaction mixture hydrolysing **10a-c**.

B. Reaction of **6a,c,d** with *t*-Butylamine/Potassium Permanganate.

Treatment of a solution of **6a,c,d** in *t*-butylamine with potassium permanganate at room temperature gives in reasonable-to-good yields the corresponding 4-(*t*-butylamino)pteridines **14a,c,d** (**14a**, 70%; **14c**, 75%; **14d**, 50%), together with the respective pteridin-4-ones **15a,c,d** (**15a**, 26%; **15c**, 18%; **15d**, 27%). No indication for the formation of a pyrazine derivative was obtained, as observed in the reactions with ethylamine (see above in section A). The structure of compounds **14a,c,d** was proved by the ir, ^{1}H nmr and mass data. The NH absorption frequency in the ir spectrum and the chemical shift values of the ring hydrogens are nearly identical with those reported for the 4-(ethylamino)pteridines **8** (see Table 1). One of the structures *i.e.* 7-*t*-butyl-4-(*t*-butylamino)-pteridine (**14d**) was confirmed by conversion into the known compound 7-*t*-butylpteridin-4-one (**15d**), using 6*N* hydrochloric acid.



Scheme 3

Attempts to measure at room temperature the supposed intermediaries in this *t*-butylamino-oxidation reaction, *i.e.* the 4-(*t*-butylamino)-3,4-dihydropteridines **16a,b,c,** were not successful. At room temperature a solution of **6a** in liquid ammonia only gives traces of **16a**; mainly the signals, characteristic for the starting material **6a** are observed. However, when the temperature is decreased to -10°, the concentration of **16a** increases and at -40° only the peaks of **16a** are present (see Table 1). This result indicates that at room temperature the equilibrium **6a** ⇌ **16a** is far to the left and at -40° far to the right. That at room temperature in about 70% yield the 4-(*t*-butylamino)pteridine **14a** is still formed indicates that in the presence of the oxidant the equilibrium **6a** ⇌ **16a** shifts to the right due to the conversion of **16a** into **14a**.

A similar temperature dependency on the equilibrium starting material ⇌ *t*-butylamino-adduct was observed with **6c,d**. Dissolved in *t*-butylamine at room temperature both compounds do not yield a σ-adduct. However, lower-

Table 1

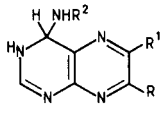
^{1}H NMR Spectral Data (δ-values)

Pteridine	H-2	H-4	H-6	Solvent
7-phenyl-(**6a**)	9.62 (s) [a]	9.74 (s)	9.60 (s) [a]	A
4-ethylamino-3,4-dihydro-7-phenyl-(**7a**)	[c]	5.49 (s)	8.75 (s)	B
4-ethylamino-7-phenyl-(**8a**)	8.62 (s)	–	9.42 (s)	C
7-*p*-methoxyphenyl-(**6b**) [b]	9.60 (s)	9.70 (s)	9.52 (s)	A
4-ethylamino-3,4-dihydro-7-*p*-methoxyphenyl-(**7b**)	7.53 (s)	5.44 (s)	8.67 (s)	B
4-ethylamino-7-*p*-methoxyphenyl-(**8b**)	8.60 (s)	–	9.37	C
6,7-diphenyl-(**6c**)	9.60 (s)	9.78 (s)	–	A
4-ethylamino-3,4-dihydro-6,7-diphenyl-(**7c**)	[c]	5.50 (s)	–	B
4-ethylamino-6,7-diphenyl-(**8c**)	8.60 (s)	–	–	C
4-*t*-butylamino-3,4-dihydro-7-phenyl-(**16a**)	[c]	5.58 (d) (J ~ 7.5 Hz)	8.65 (s)	D
4-*t*-butylamino-7-phenyl-(**14a**)	8.62 (s)	–	9.35 (s)	C
4-*t*-butylamino-3,4-dihydro-6,7-diphenyl-(**16b**)	[c]	5.58 (d) (J ~ 6 Hz)	–	D
4-*t*-butylamino-6,7-diphenyl-(**14c**)	8.70 (s)	–	–	A
7-*t*-butyl-(**6d**)	9.49 (s)	9.59 (s)	9.12 (s)	A
4-*t*-butylamino-3,4-dihydro-7-*t*-butyl-(**16c**)	7.23 (s)	5.49 (d) (J ~ 6 Hz)	8.14 (s)	D
4-*t*-butylamino-7-*t*-butyl-(**14d**)	8.66 (s)	–	8.66 (s)	A
4-*n*-propylamino-3,4-dihydro-7-phenyl-(**16d**)	[c]	5.45 (s)	8.70 (s)	E
4-*n*-propylamino-3,4-dihydro-7-*p*-methoxyphenyl-(**16e**)	7.50 (s)	5.43 (s)	8.63 (s)	E
4-*n*-propylamino-3,4-dihydro-6,7-diphenyl-(**16f**)	[c]	5.49 (s)	–	E
4-*n*-propylamino-3,4-dihydro-7-*t*-butyl-(**16g**)	7.43 (s)	5.38 (s)	8.20 (s)	E
4-*n*-butylamino-3,4-dihydro-7-phenyl-(**16h**)	[c]	5.44 (s)	8.65 (s)	F
4-*n*-butylamino-3,4-dihydro-7-*p*-methoxyphenyl-(**16i**)	7.50 (s)	5.43 (s)	8.60 (s)	F
4-*n*-butylamino-3,4-dihydro-6,7-diphenyl-(**16j**)	[c]	5.45 (s)	–	F
4-*n*-butylamino-3,4-dihydro-7-*t*-butyl-(**16k**)	7.47 (s)	5.40 (s)	8.20 (s)	F

A - deuteriochloroform, B - ethylamine, C - d6-dimethylsulfoxide, D - *t*-butylamine, E - *n*-propylamine, F - *n*-butylamine. Absorptions for the protons of *N*-ethyl group: δ = 1.25 (3H, tr, CH_3) (**8a-8c**); 3.7 (**8a**), 3.65 (**8b**,**8c**) (2H, dq, CH_2). For *N*-t-butyl group: δ = 1.6 (**14a**,**14d**), 1.55 (**14c**) (9H, s, (CH_3).

[a] May be interchanged. [b] Due to its high insolubility in *t*-butylamine no resonance signals have been recorded at -10°, -40°, as well as when the solution is allowed to be at room temperature. [c] Could not be detected because of signal overlap by the phenyl protons.

ing the temperature of the solution to -40° adduct **16b** is nearly quantitatively formed from **6c**. The conversion of **6d** into **16c** is already completed at -20°.



16

	R	R^1	R^2
a)	C_6H_5	H	t-C_4H_9
b)	C_6H_5	C_6H_5	t-C_4H_9
c)	t-C_4H_9	H	t-C_4H_9
d)	C_6H_5	H	n-C_3H_7
e)	p$OCH_3C_6H_4$	H	n-C_3H_7
f)	C_6H_5	C_6H_5	n-C_3H_7
g)	t-C_4H_9	H	n-C_3H_7
h)	C_6H_5	H	n-C_4H_9
i)	p$OCH_3C_6H_4$	H	n-C_4H_9
j)	C_6H_5	C_6H_5	n-C_4H_9
k)	t-C_4H_9	H	n-C_4H_9

Scheme 4

This interesting difference in temperature dependency on adduct formation at C-4 in pteridines between *t*-butylamine and ethylamine induced us to carry out a few initial experiments concerning the addition of *n*-propylamine and *n*-butylamine to the pteridines **6a-d**. We found that the compounds **6a-d**, when dissolved in those alkylamines at room temperature, are nearly quantitatively converted into their respective adducts **16d-k**, as observed by ^{1}H nmr spectroscopy (see Table 1). The chemical shifts of the ring hydrogens in these adducts are in good accordance with those found for **7a-c** and **16a-c**. Lowering the temperature of these solutions from room temperature to -40° usually leads to a nearly complete disappearance of the adduct signals and formation of some decomposition products.

The interesting phenomena why the *t*-butylamino adducts **16a-c** dissociate at room temperature so easily into their respective pteridines while the adducts formed from pteridines and unbranched alkylamines are stable at room temperature is a matter of further investigations.

EXPERIMENTAL

Melting points are uncorrected. The ir spectra were obtained as potassium bromide pellets using spectrometer A-100 (Jasco). The ^{1}H nmr spectra were recorded on Hitachi Perkin-Elmer R-24B (60 MHz) and

Varian EM-390 (90 MHz) spectrometers with TMS as internal standard. The mass spectra were obtained on AEJ MS-902. For the column chromatography silicagel 60 (70-230 mesh ASTM) Merck was used.

General Procedure for the Amination of Pteridines **6a-6d** by Primary Amines.

a) By Ethylamine.

To a stirred solution of ethylamine (about 20 ml) containing 158 mg (1 mmole) of potassium permanganate 1 mmole of the corresponding pteridine **6a-6c** was added in one portion. The stirring was continued for 6 hours at the temperature of about 16 ~ 17°. Then methanol (25 ml) was added and the mixture was allowed to stand overnight. After filtration by suction, the brown precipitate (manganese dioxide) was washed with methanol. To the methanol solution silicagel (about 1-1.5 g) was introduced and the solvent was evaporated to dryness under reduced pressure. Chromatography of the residue on silicagel and elution with chloroform gave at first the compounds **11a-11c**, then the ethylamino derivatives **8a,8c**, respectively. Only in the case of the compound **8b** further elution with methanol-chloroform mixture (0.5:9.5) was applied.

b) By *t*-Butylamine.

The reaction was performed in the same way as described in section a, using for 1 mmole of the corresponding pteridine **6a,6c,6d** 158 mg (1 mmole) of potassium permanganate and 25-30 ml of *t*-butylamine. The obtained compounds were purified on the column filled with silicagel. Elution with chloroform gave compounds **14a,14c,14d**, respectively. Further elution with methanol-chloroform mixture (0.5:9.5) gave the corresponding pteridin-4-ones **15a,15c,15d**.

Reaction of **6a** with Ethylamine/Potassium Permanganate.

4-(Ethylamino)-7-phenylpteridine (**8a**).

This compound was obtained in a yield of 26%, pale yellow crystals, mp, 234-235° (from chloroform/light petroleum bp, 60-80°); ms: m/e 251 (M^+), ir = 3275 cm^{-1} (NH).

Anal. Calcd. for $C_{14}H_{13}N_5$ (251.28): C, 66.91; H, 5.21. Found: C, 67.21; H, 5.23.

2-Amino-3-formyl-6-phenylpyrazine (**11a**).

This compound was obtained in a yield of 38%, yellow crystals, mp, 200-202° (from chloroform); ms: m/e 199.0743 (M^+) (Calcd. 199.0746), ir = 3400, 3275 (NH_2), 1690 cm^{-1} (CO); ^1H nmr (deuteriochloroform): δ = 10.5 (1H, s, C*H*O), 8.52 (1H, s, H-5), 7.55-7.35 (3H, m, phenyl), 8.20-7.95 (2H, m, phenyl).

Anal. Calcd. for $C_{11}H_9N_3O$ (199.21): C, 66.32; H, 4.55. Found: C, 66.28; H, 4.53.

Reaction of **6a** with Ethylamine Without Potassium Permanganate.

2-Amino-3-(ethyliminomethylene)-6-phenylpyrazine (**10a**).

Compound **6a** (208 mg, 1 mmole) was treated with about 8 ml of anhydrous ethylamine at room temperature for 4 hours. Then ethylamine was evaporated at room temperature and the residue was crystallized from light petroleum bp, 40-60°. The separated crystals were filtered off, yield 78%, mp, 120-121°; ms: m/e 226.1217 (calcd. 226.1218), ir: 3325, 3250 (NH_2), 1640 cm^{-1} (>C = N-). ^1H nmr (deuteriochloroform): δ = 8.50-8.44 (1H, tr, -C*H*=N-CH_2CH_3, J C*H*=N-CH_2 = 1.2 Hz), 8.4 (1H, s, 5-H), 8.1-7.9 (2H, m, phenyl), 7.55-7.35 (3H, m, phenyl), 7.4-7.00 (2H, N*H*$_2$), 3.85-3.5 (2H, dq, C*H*$_2$, J CH_2CH_3 = 7.2 Hz), 1.4-1.9 (3H, tr, C*H*$_3$).

Anal. Calcd. for $C_{13}H_{14}N_4$ (226.27): C, 69.00; H, 6.24. Found: C, 69.08; H, 6.28.

Reaction of **6b** with Ethylamine/Potassium Permanganate.

4-(Ethylamino)-7-*p*-methoxyphenylpteridine (**8b**).

This compound was obtained in a yield of 36%, pale yellow crystals, mp, 220-221° (from chloroform/ether); ms: m/e 281 (M^+), ir: 3210 cm^{-1} (NH).

Anal. Calcd. for $C_{15}H_{15}N_5O$ (281.31): C, 64.04; H, 5.37. Found: C, 64.43; H, 5.44.

2-Amino-3-formyl-6-*p*-methoxyphenylpyrazine (**11b**).

This compound was obtained in a yield of 18%, yellow crystals, mp, 209-211° (from chloroform); ms: m/e 229.0856 (M^+) (Calcd. 229.0851); ir: 3385, 3260 (NH_2), 1680 cm^{-1} (CO); ^1H nmr (d6-dimethylsulfoxide): δ = 10.00 (1H, s, C*H*O), 8.65 (1H, s, H-5), 8.40-8.10 (2H, d, phenyl), 7.30-7.05 (2H, d, phenyl), 3.87 (3H, s, C*H*$_3$), 7.90-7.60 (2H, N*H*$_2$).

Anal. Calcd. for $C_{12}H_{11}N_3O_2$ (229.23): C, 62.87; H, 4.83. Found: C, 63.07; H, 4.86.

Reaction of **6c** with Ethylamine/Potassium Permanganate.

4-(Ethylamino)-6,7-diphenylpteridine (**8c**).

This compound was obtained in a yield of 14%, pale yellow crystals, mp, 160-162° (from light petroleum bp, 60-80°); ms: m/e 327 (M^+), ir = 3220 cm^{-1} (NH).

Anal. Calcd. for $C_{20}H_{17}N_5$ (327.38): C, 73.37; H, 5.23. Found: C, 73.16; H, 5.16.

2-Amino-3-formyl-6,7-diphenylpyrazine (**11c**).

This compound was obtained in a yield of 43%, yellow crystals, mp, 182-184° (from light petroleum bp, 80-100°); ms: m/e 275.1061 (M^+) (Calcd. 275.1051), ir: 3400, 3250 (NH_2), 1670 cm^{-1} (CO); ^1H-nmr (deuteriochloroform): δ 10.12 (1H, s, C*H*O), 7.55-7.18 (10H, m, phenyl), 7.00-7.65 (2H, NH_2).

Anal. Calcd. for $C_{17}H_{13}N_3O$ (275.30): C, 74.16; H, 4.76. Found: C, 74.45; H, 4.77.

Reaction of **6a** with *t*-Butylamine/Potassium Permanganate.

4-(*t*-Butylamino)-7-phenylpteridine (**14a**).

This compound was obtained in a yield of 70%, yellow crystals, mp, 135-137° (from light petroleum, bp, 60-80°); ms: m/e 279 (M^+), ir: 3375 cm^{-1} (NH).

Anal. Calcd. for $C_{16}H_{17}N_5$ (279.34): C, 68.79; H, 6.13. Found: C, 68.69; H, 6.21.

7-Phenylpteridin-4-one (**15a**).

This compound was obtained in a yield of 26%; ms: m/e 224 (M^+). This compound was identical with the product obtained previously [1,3].

Reaction of **6c** with *t*-Butylamine/Potassium Permanganate.

4-(*t*-Butylamino)-6,7-diphenylpteridine (**14c**).

This compound was obtained in a yield of 75%, pale yellow crystals, mp, 204-206° (from light petroleum bp, 60-80°); ms: m/e 355 (M^+), ir: 3375 cm^{-1} (NH).

Anal. Calcd. for $C_{22}H_{21}N_5$ (355.43): C, 74.34; H, 5.96. Found: C, 74.04; H, 5.91.

6,7-Diphenylpteridin-4-one (**15c**).

This compound was obtained in a yield of 18%; ms: m/e 300 (M^+). This compound was identical in all respects with an authentic sample [1,4,5].

Reaction of **6d** with *t*-Butylamine/Potassium Permanganate.

4-(*t*-Butylamino)-7-*t*-butylpteridine (**14d**).

This compound was obtained in a yield of 50%, colourless crystals, mp, 105-106° (from light petroleum bp, 60-80°); ms: m/e 259 (M^+); ir: 3325 cm^{-1} (NH).

Anal. Calcd. for $C_{14}H_{21}N_5$ (259.35): C, 64.83; H, 8.16. Found: C, 65.12; H, 8.34.

7-*t*-Butylpteridin-4-one (**15d**).

This compound was obtained in a yield of 27%; ms: m/e 204 (M^+). Compound **15d** was identical in all respects with an authentic sample [1,6].

2-Amino-6-phenylpyrazine-3-carboxylic Acid (**12**).

To a suspension of 25 mg (0.125 mmole) of compound **11a** in 2 ml of water, 3 ml of 0.1 *M* solution of potassium permanganate was slowly add-

ed. The mixture was stirred for 1 hour at room temperature, then boiled and filtered. The filtrate was acidified by acetic acid. The separated crystals (28%) were filtered off and dried, mp, 234-236° dec, lit [7] 225° dec; ir: 3440, 3250 (NH_2), 2500-3200 (CO*OH*), 1675 (CO); ms: m/e 215.06949 (M^+) (Calcd. 215.06947).

Acid **12** is dissolved in the solution of sodium bicarbonate. The residue on the filter was exhaustively extracted with boiling chloroform. After evaporation of the solvent the substance (22%) proved to be the starting material.

2-Amino-6-phenylpyrazine (**13**).

Some crystals of acid **12** were heated to melt and maintained at this temperature for about 2 minutes. After cooling the residue was dissolved in chloroform. Evaporation of the solvent *in vacuo* gave 2-amino-6-phenylpyrazine (**13**), mp, 123-125°, lit [7] mp, 125-126°; ms: m/e 171 (M^+).

Hydrolysis of Compound **14d** into 7-*t*-Butylpteridin-4-one (**15d**).

Compound **14d** (100 mg, 0.386 mmole) was treated with 5 ml of 6*N* hydrochloric acid and heated under reflux for 15 minutes. After cooling the separated crystals were filtered off, washed with water until the acidic reaction disappeared and dried, 40 mg (51% yield) of colourless crystals were obtained, mp, >300° dec, after reprecipitation from a dilute solution of sodium hydroxide by acetic acid. Ir spectrum of this substance was identical with **15d**, obtained previously [1,6].

Acknowledgement.

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