Contribution to Methylation of 9-Alkylxanthines

A. BOZÓOVÁ, A. RYBÁR*, J. ALFÖLDI, V. PÄTOPRSTÝ,
M. KAČURÁKOVÁ, and V. LOKAJ

Institute of Chemistry, Slovak Academy of Sciences, SK-842 38 Bratislava

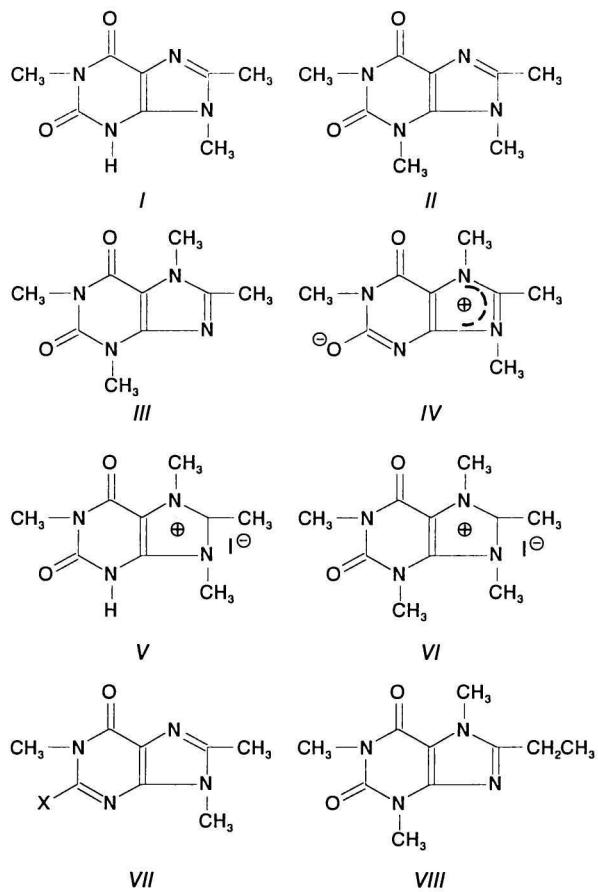
Received 16 November 1992

Chromatographic and spectral methods were the tools for investigation of the methylation products of the reaction of 1,8,9-trimethylxanthine with methyl iodide in dimethylformamide in the presence of potassium carbonate. In addition to the expected 1,3,8,9-tetramethylxanthine also products of consecutive reactions — 1,3,7,8-tetramethylxanthine, 1,7,8,9-tetramethylxanthinium betaine, 1,7,8,9-tetramethylxanthinium iodide, 1,3,7,8,9-pentamethylxanthinium iodide and little amounts of 2-methoxy-1,8,9-trimethylhypoxanthine and 8-ethyl-1,3,7-trimethylxanthine — were separated and identified.

Experiments to prepare 1,3,8,9-tetramethylxanthine (*II*) from 1,8,9-trimethylxanthine (*I*) gave repeatedly the required product *II* in low ≈ 33 % yields. More detailed investigation of this methylation employing chromatographic and spectral methods and standards synthesized by alternative methods, enabled us to determine the structure of by-products and thereby to consider the reaction course and consequently, the reason for low yield of compound *II*.

Methylation of 9-methylxanthines was reported in two papers [1, 2]: 1,9-dimethylxanthine treated with methyl *p*-toluenesulfonate (serving as reaction medium) in the mole ratio x_r = 1 : 10 at 130 °C afforded 1,7,9-trimethylxanthinium tosylate [1] in line with the known results of the alkylation of xanthines in neutral or slightly acid media [3]. 1,9-Dimethyl-, 1-methyl-9-propyl-, and 1-methyl-9-(2-phenylethyl)-8-phenylxanthines and methyl iodide in dimethylformamide (x_r = 1 : 10) in the presence or absence of potassium carbonate at about 150 °C all yielded 1,3,7-trimethyl-8-phenylxanthine instead of the expected 1,3,9-trimethyl-, 1,3-dimethyl-9-propyl- or 1,3-dimethyl-9-(2-phenylethyl) derivatives [2]. This methylation in positions 3 and 7 is accompanied with a thermal elimination of the alkyl group from position 9 in the form of an alkyl iodide.

Alkylation of xanthines with methyl iodide in dimethylformamide in the presence of potassium carbonate we already used [4, 5] has also been applied for methylation of compound *I*; this procedure differs from that described in Ref. [2] by a substantially lower reaction temperature (80 °C) and excess of methyl iodide. As found, the main methylation product of compound *I* is, as expected, tetramethyl derivative *II*, nevertheless the reaction did not proceed unambiguously, because a number of further products was obtained. Thus, the main reaction products at the xanthine *I* to methyl iodide to potassium carbonate mole ratio x_r = 1.0 : 1.2 : 1.2 were, in addition to the intact starting compound *I* (14.6 %) (composition in mass %), 1,3,8,9-tetramethyl derivative *II* (47.8 %), 1,3,7,8-tetramethylxanthine (*III*, 17.8 %), 1,7,8,9-tetramethylxanthinium betaine (*IV*, 6.0 %), 1,7,8,9-tetramethylxanthinium iodide (*V*, 3.2 %) and 1,3,7,8,9-pentamethyl-



I *II* *III* *IV* *V* *VI* *VII* *VIII*

VIIa X = OH
VIIb X = Cl
VIIc X = CH_3O

*The author to whom the correspondence should be addressed.

Table 1. Retention Time (t_R), Capacity Factor (c), and Resolution Factor (R_{jl}) of Compounds *I*—*VIII*

Compound	t_R/min	c^a	R_{jl}
VI	2.659	0.87	
			1.62
I	7.575	4.33	
			1.53
IV	10.829	6.62	
			1.20
V	13.183	8.28	
			1.58
II	22.100	14.56	
			1.53
III	26.895	17.94	
			1.60
VIIc	32.942	22.19	
			1.45
VIII	39.726	26.97	

a) $c = \frac{t_R - t_0}{t_0}$; dead time $t_0 = 1.42$ min.

xanthinium iodide (*VI*, 8.5 %) besides of a small amount of 2-methoxy-1,8,9-trimethylhypoxanthine (*VIIc*, 1.0 %) and 8-ethyl-1,3,7-trimethylxanthine (*VIII*, 1.1 %). At the same reaction conditions, but with the doubled methyl iodide mole ratio (*i.e.* $x_r = 1.0 : 2.4 : 1.2$) composition of the reaction mixture changed as follows: content of derivative *III* increased substantially (40.7 %), that of compound *II* decreased (15.2 %), mass fraction of further components also changed: betaine *IV* (13.7 %), quaternary 1,7,8,9-tetramethyl derivative *V* (13.0 %), quaternary 1,3,7,8,9-pentamethyl derivative *VI* (11.7 %), 8-ethyl-1,3,7-trimethylderivative *VIII* (3.1 %), 2-methoxy derivative *VIIc* (0.9 %) and the starting compound *I* (1.7 %). The above-mentioned content represents the average values of five measurements in both series with a relative error not exceeding ± 5 %. These values are based on analytical HPLC. Chromatographic parameters of compounds under study are listed in Table 1. Compounds *II*, *III*, and *IV* were isolated from the mixture by crystallization, the betaine *IV* and xanthinium iodide *V* mixture was separated by a preparative HPLC. The originally considered $w(IV) : w(V)$ ratio was deduced from the iodine content determined; later this ratio and also that of other compounds in the mixture was determined by gradient chromatography performed on an efficient chromatographic column. Methoxy derivative *VIIc* and 8-ethyl-1,3,7-trimethyl derivative *VIII* could not be separated by crystallization; they were obtained from mother liquors after removing products *II* to *VI* by iterative separation of the appropriate fraction on preparative HPLC.

Tetramethyl derivative *II* is the expected alkylation product of the starting 1,8,9-trimethylxanthine *I* with methyl iodide in dimethylformamide in the presence of alkaline reagents (in contrast with conditions given in paper [2]). To ascertain its structure, compound *II* having the methyl group reliably in the position 3 was prepared from 6-methylamino-1,3-dimethyluracil *via* its 5-nitroso and 5-amino derivatives, and by cyclization of the latter with ethyl orthoacetate under acid catalysis. Both products were proved to be chromatographically and spectrally identical.

Betaine *IV* can be formed only by elimination of hydrogen iodide during the reaction through the intermediary xanthinium iodide *V* due to the presence of potassium carbonate. To evidence the structure of betaine *IV* and to prove our hypothesis on its formation, we synthesized the corresponding xanthinium iodide *V* from the starting compound *I* by heating with methyl iodide in dimethylformamide (*cf.* the formation of like compounds in Ref. [6]). The iodide *V* can be converted into betaine *IV* with alkaline reagents as *e.g.* potassium carbonate, ammonia, or, most carefully with silver acetate. Betaine *IV* was also obtained when the reaction was carried out with the mixture of compounds *IV* and *V* isolated by preparative HPLC. Compounds *IV* and *V* prepared by the afore-mentioned synthesis and betaine *IV* are both chromatographically and the latter also spectrally identical with the corresponding compounds from the reaction mixture.

1,3,7,8-Tetramethyl derivative *III* could originate by rearrangement of the methyl group from the position 9 to the position 7. We presume in accordance with Ref. [2] that the first step involves formation of the quaternary 1,3,7,8,9-pentamethyl derivative *VI* from which methyl (from N-9) iodide was thermally eliminated. This assumption was verified through the synthesis of the quaternary pentamethyl derivative *VI* from 1,3,8,9-tetramethyl derivative *II* by heating with methyl iodide in dimethylformamide at reflux temperature in the absence of potassium carbonate. Compound *III* prepared in this way was proved to be chromatographically and spectrally identical with the product *III* isolated from the mixtures after methylation of compound *I* and that prepared from 8-methyltheophylline according to Ref. [4]. Compound *III* is the main product (80 % in the distillation residue of the reaction mixture) which can be obtained also by heating of 1,3,8,9-tetramethyl derivative *II* with methyl iodide in dimethylformamide ($x_r = 1.0 : 1.2$) at 150 °C in a closed vessel without isolation of the quaternary pentamethyl compound *VI*. As found, heating of the latter at 80 °C in dimethylformamide in the presence or absence of potassium carbonate furnished 1,3,8,9-tetramethyl derivative *II* as the main product (90 % in the distillation residue of the reaction mixture), small amounts of 1,3,7,8-tetramethyl derivative *III* (7 %) and the starting compound *VI*. Compound *II* originated in this reaction as a result of elimination of methyl iodide from the quaternary pentamethyl de-

rivative *VI*, but the leaving methyl group stemmed from nitrogen N-7. This is a substantial difference between the behaviour of 9-methyl-8-phenylxanthine (Ref. [2]) and our 8,9-dimethylxanthine *I* during methylation.

It is worth noting that also 8-ethyl-1,3,7-trimethylxanthine (*VIII*) was obtained in a small amount when methylating the starting compound *I*. We rationalize this result by formation of a C-anion from the methyl group of compound *III* in the position 8 and a subsequent methylation. This assumption is supported by the experiment in which the quaternary pentamethyl derivative *VI* was heated in dimethylformamide with a further equivalent of methyl iodide in the presence of potassium carbonate at 150 °C for 5 h. Content of the 8-ethyl derivative *VIII* and the primarily originating 8-methyl derivative *III* in the distillation residue was found to be 35 and 60 %, respectively. Structure of the 8-ethyl derivative *VIII* was corroborated analogously with the preceding determinations, through identity of its chromatographic and spectral data with those of that synthesized from 8-ethinyl-1,3-dimethylxanthine [7].

2-Methoxy-1,8,9-trimethylhypoxanthine (*VIIc*) as a methylation product of the enol form of compound *I* (*VIIa*) was anticipated among the methylation products of the starting derivative *I*. 2-Methoxy derivative *VIIc* originated under both alkylation procedures in 0.9 to 1.0 % yields only. To identify unambiguously the hypoxanthine *VIIc* a specimen was synthesized from compound *I*, which was treated with phosphoryl chloride to give the 2-chloro product *VIIb*; its methoxylation with sodium methoxide gave compound *VIIc* chromatographically and spectrally identical with the isolated one.

EXPERIMENTAL

Melting points are uncorrected. Samples for analysis were dried over phosphorus pentaoxide at 100 °C and 130 Pa for 8 h. The mass spectra were measured with a Jeol 100-D spectrometer at 70 eV ionization energy and the IR spectra of KBr pellets were taken with a Perkin—Elmer, model G 983 spectrophotometer. The ^{1}H and ^{13}C NMR spectra of compounds in DMSO-d_6 were recorded with a Bruker AM-300 apparatus at 300 MHz and 75 MHz, respectively, tetramethylsilane being the internal reference. Reaction courses, composition of the appropriate fractions of the preparative separations and the purity of compounds under examination were monitored by HPLC with a Hewlett—Packard, model 1050 instrument employing a column (0.4 cm × 25.0 cm) packed with Separon SGX C18, grain size 5 μm, flow rate 1.0 cm^3 min^{-1}, mobile phase: methanol—water—tetrahydrofuran, gradient elution from φ_r = 5 : 95 : 0 to φ_r = 50 : 49 : 1, detection by UV 220 nm. Preparative HPLC was carried out with a Waters Delta Prep 3000 instrument using a column (4.7 cm × 30 cm) packed with Delta PAK C18, grain size 15 μm, flow rate 15 cm^3 min^{-1}, mobile phase: methanol—water (φ_r = 40 : 60), detection by UV 220 nm. Content of the individual compounds in their mixtures, obtained by analytical HPLC, was expressed in mass fraction.

1,8,9-Trimethylxanthine (*I*)

p-Toluenesulfonic acid (50 mg) and ethyl orthoacetate (16.2 cm^3, 14.3 g, 88.0 mmol) were added to a suspension of 5-amino-6-methylamino-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (Ref. [8], 10.0 g, 58.8 mmol) in dimethylformamide (50 cm^3); the mixture was refluxed with stirring for 3 h. Ethanol (100 cm^3) was then added, the content was refluxed for additional 30 min, cooled to room temperature, the separated product was filtered off and crystallized from ethanol. Yield 8.0 g (70 %), m.p. = 338—341 °C (Ref. [2] gives m.p. = 340 °C). ^{1}H NMR spectrum, δ: 2.39 (s, 3H, C-8—CH_3), 3.25 (s, 3H, N-1—CH_3), 3.62 (s, 3H, N-9—CH_3), 12.19 (s, 1H, N-3—H). ^{13}C NMR spectrum, δ: 12.9 (C-8—CH_3), 27.0 (N-1—CH_3), 30.0 (N-9—CH_3).

1,3,8,9-Tetramethylxanthine (*II*)

Method A: Compound *I* (1.01 g; 5.2 mmol), potassium carbonate (0.85 g; 6.2 mmol), and methyl iodide (0.39 cm^3, 0.89 g, 6.2 mmol) were heated to 80 °C in dimethylformamide (15 cm^3) with stirring in a closed glass vessel for 5 h. Dimethylformamide was distilled off under diminished pressure and the residue was refluxed in chloroform (20 cm^3) for 30 min. The mixture was cooled to room temperature, the insoluble portion was filtered off, the filtrate was concentrated under reduced pressure and the dry distillation residue was crystallized from ethanol and recrystallized from acetone—ethanol. Yield 0.35 g (33 %), m.p. = 268—270 °C (Ref. [9] gives m.p. = 263 °C).

Method B: 5-Amino-6-methylamino-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione (Ref. [10], 5.0 g, 27 mmol), *p*-toluenesulfonic acid (10 mg), and ethyl orthoacetate (7.5 cm^3, 6.6 g, 41 mmol) were heated in dimethylformamide (25 cm^3) at 85 °C for 1.5 h. The product filtered off from the cooled mixture was crystallized from acetone—ethanol. Yield 3.7 g (66 %), m.p. = 269—271 °C. Mass spectrum, *m/z*: 208 (M^+). IR spectrum, $\tilde{\nu}$/cm^{-1}: 1965, 1645 (2 × C=O). ^{1}H NMR spectrum, δ: 2.44 (s, 3H, C-8—CH_3), 3.30 (s, 3H, N-1—CH_3), 3.76 (s, 3H, N-3—

CH_3), 3.90 (s, 3H, N-9—CH_3), ^{13}C NMR spectrum, δ: 13.7 (C-8—CH_3), 28.1 (N-1—CH_3), 31.2 (N-3—CH_3), 32.9 (N-9—CH_3).

1,3,7,8-Tetramethylxanthine (*III*)

Method A: Compound *I* (1.01 g; 5.2 mmol), potassium carbonate (0.85 g; 6.2 mmol), methyl iodide (0.78 cm^3, 1.76 g, 12.4 mmol), and dimethylformamide (15 cm^3) were heated to 80 °C in a closed glass vessel with stirring for 5 h. The solvent was distilled off under diminished pressure and the residue was refluxed with chloroform (25 cm^3) for 30 min. The insoluble portion was filtered off from the cooled mixture and the filtrate was evaporated to dryness under reduced pressure and the residue was crystallized from ethanol. Yield 0.40 g (37 %), m.p. = 214—215 °C (Ref. [11] gives m.p. = 211—213 °C).

Method B: Compound *VI* (0.35 g; 1.0 mmol) was heated to 160 °C in dimethylformamide (10 cm^3) with stirring for 2 h. The solvent was removed *in vacuo* and the residue was twice crystallized from ethanol. Yield 0.15 g (75 %), m.p. = 213—214 °C. Mass spectrum, *m/z*: 208 (M^+). IR spectrum, $\tilde{\nu}/cm^{-1}$: 1756, 1713 (2 × C=O). ^1H NMR spectrum, δ: 2.49 (s, 3H, C-8—CH_3), 3.30 (s, 3H, N-1—CH_3), 3.47 (s, 3H, N-3—CH_3), 3.90 (s, 3H, N-7—CH_3). ^{13}C NMR spectrum, δ: 12.7 (C-8—CH_3), 27.4 (N-1—CH_3), 29.3 (N-3—CH_3), 31.5 (N-7—CH_3).

1,3,8,9-Tetramethylxanthinium Betaine (*IV*) and 1,3,8,9-Tetramethylxanthinium Iodide (*V*)

Method A: The insoluble portions from extraction of the distillation residue with chloroform obtained from five preparation experiments of compound *II* (method *A*) refluxed in dry ethanol for 10 min were hot filtered to remove inorganic salts; the filtrate was evaporated to dryness under diminished pressure and the residue containing compounds *I* (6.0 %), *II* (19.5 %), *IV* (35.1 %), *V* (21.0 %), and *VI* (18.4 %) was dissolved in the mobile phase and separated by preparative HPLC monitored by analytical HPLC. A glassy product (350 mg), which crystallized within 24 h, composed of compounds *IV* (62 %) and *V* (37 %), was separated after removing compounds *I*, *II*, and *VI*.

Method B: Compound *I* (2.0 g; 10.3 mmol) and methyl iodide (2.0 cm^3, 4.6 g, 31.5 mmol) were stirred and heated to 80 °C in dimethylformamide (20 cm^3) for 2 h. The solvent was distilled off under reduced pressure and the residue was crystallized from methanol. Yield 2.2 g of compound *V* (64 %), m.p. = 255—257 °C. For $C_9H_{13}N_4O_2$ (M_r = 336.1) w_i(calc.): 32.16 % C, 3.90 % H, 37.76 % I, 16.67 % N; w_i(found): 31.92 % C, 3.99 % H, 37.21 % I, 16.89 % N. IR spectrum, $\tilde{\nu}/cm^{-1}$: 1718, 1656 (2 × C=O). ^1H NMR spectrum, δ: 2.68 (s, 3H, C-8—CH_3), 3.20 (s, 3H, N-1—CH_3), 3.73 (s, 3H, N-7—CH_3), 3.98 (s, 3H, N-9—CH_3). ^{13}C NMR spectrum, δ: 10.1 (C-8—CH_3), 27.4 (N-1—CH_3), 32.0 (N-9—CH_3), 33.4 (N-7—CH_3).

Method C: Compound *V* (335 mg; 1.0 mmol), potassium carbonate (170 mg; 1.2 mmol), and dimethylformamide (10 cm^3) were heated to 80 °C for 5 h. Dimethylformamide was then removed *in vacuo* and the residue was refluxed with dry ethanol (15 cm^3). A small amount of potassium iodide separating on cooling was filtered off, the filtrate was concentrated to 1/4 of its original volume and allowed to crystallize. Yield 143 mg of compound *IV* (69 %), m.p. = 296—299 °C.

Method D: Compound *V* (335 mg; 1.0 mmol) and silver acetate (167 mg; 1.0 mmol) were stirred in distilled water (15 cm^3) at ambient temperature for 5 h. Silver iodide was filtered off, the filtrate was evaporated to dryness under reduced pressure and the residue was crystallized from ethanol. Yield of compound *IV* was 160 mg (80 %), m.p. = 297—300 °C. For $C_9H_{12}N_4O_2$ (M_r = 208.2) w_i(calc.): 51.91 % C, 5.81 % H, 26.91 % N; w_i(found): 51.69 % C, 5.63 % H, 27.06 % N. Mass spectrum, *m/z*: 208 (M^+). IR spectrum, $\tilde{\nu}/cm^{-1}$: 1681 (C=O). ^1H NMR spectrum, δ: 2.64 (s, 3H, C-8—CH_3), 3.21 (s, 3H, N-1—CH_3), 3.59 (s, 3H, N-7—CH_3), 3.99 (s, 3H, N-9—CH_3). ^{13}C NMR spectrum, δ: 9.35 (C-8—CH_3), 27.1 (N-1—CH_3), 28.5 (N-9—CH_3), 32.3 (N-7—CH_3).

1,3,7,8,9-Pentamethylxanthinium Iodide (*VI*)

Method A: The insoluble portions from extraction of the distillation residue with chloroform, obtained from five preparation experiments of compound *III* (method *A*) were refluxed with dry ethanol (10 cm^3) for 10 min, hot-filtered to remove the inorganic salts and the filtrate was evaporated to dryness *in vacuo*. The residue containing compounds *I* (3.1 %) and *VI* (96.8 %) was dissolved in dry ethanol (8 cm^3), a small amount of potassium iodide and the starting compound *I* separating on cooling were filtered off, the filtrate was concentrated to 1/5 of its original volume and left to crystallize. Yield 439 mg of compound *VI*, m.p. = 171—174 °C.

Method B: A stirred mixture consisting of compound *II* (1.0 g; 4.8 mmol), methyl iodide (1.0 cm^3, 2.3 g, 15.7 mmol), and dimethylformamide (10 cm^3) was heated to 80 °C in a closed vessel for 2 h. The solvent was distilled off under diminished pressure and the residue was crystallized from ethanol. Yield 1.1 g (66 %), m.p. 174—176 °C. For $C_{10}H_{15}IN_4O_2$ (M_r = 350.2) w_i(calc.): 34.30 % C, 4.32 % H, 36.24 %

I, 16.00 % N; w_i(found): 34.08 % C, 4.42 % H, 35.97 % I, 16.34 % N. IR spectrum, $\tilde{\nu}$/cm^{-1}: 1721, 1670 (2 × C=O). ^{1}H NMR spectrum, δ: 2.87 (s, 3H, C-8—CH_3), 3.35 (s, 3H, N-1—CH_3), 3.43 (s, 3H, N-7—CH_3), 3.85 (s, 3H, N-3—CH_3), 4.15 (s, 3H, N-9—CH_3). ^{13}C NMR spectrum, δ: 10.7 (C-8—CH_3), 28.4 (N-1—CH_3), 32.2 (N-3—CH_3), 33.7 (N-9—CH_3), 35.2 (N-7—CH_3).

2-Methoxy-1,8,9-trimethylhypoxanthine (*VIIc*)

Method A: Combined mother liquors from five preparation experiments of compounds *II* and *III* each were evaporated to dryness under diminished pressure, the residue was dissolved in mobile phase and separated by preparative HPLC. The separation process was monitored by analytical HPLC; compound *VIIc* (40 mg), m.p. = 138—140 °C was obtained after removal of compounds *I* to *VI*.

Method B: Compound *I* (0.39 g; 2 mmol) was refluxed with phosphoryl chloride (5.0 cm^3, 8.2 g, 54 mmol) for 5 h. Excess of the reagent was distilled off under reduced pressure, the residue was twice extracted with chloroform—water, the chloroform layer was separated, dried with sodium sulfate and concentrated to dryness. Toluene (20 cm^3) and 1 M sodium methoxide in methanol (2 cm^3, 2 mmol) were added to the crude 2-chloro derivative *VIIb* at 0 °C. The mixture was stirred at room temperature for 7 h, the separated sodium chloride was filtered off, the toluene soluble filtrate was evaporated to dryness under diminished pressure. The residue was chromatographed on a silica gel-packed column (6 g, 100—160 μm) with chloroform—methanol (φ_r = 9 : 1) to afford compound *VIIc*, m.p. = 139—141 °C in 72 % yield (0.30 g). For $C_9H_{12}N_4O_2$ (M_r = 208.2) w_i(calc.): 51.91 % C, 5.81 % H, 26.91 % N; w_i(found): 51.68 % C, 6.00 % H, 26.80 % N. Mass spectrum, *m/z*: 208 (M$^+$). IR spectrum, $\tilde{\nu}$/cm^{-1}: 1689 (C=O). ^{1}H NMR spectrum, δ: 2.64 (s, 3H, C-8—CH_3), 3.22 (s, 3H, N-1—CH_3), 3.60 (s, 3H, C-2—OCH_3), 4.00 (s, 3H, N-9—CH_3). ^{13}C NMR spectrum, δ: 13.4 (C-8—CH_3), 27.7 (N-1—CH_3), 28.4 (N-9—CH_3), 56.0 (C-2—OCH_3).

8-Ethyl-1,3,7-trimethylxanthine (*VIII*)

The title product was isolated from the combined mother liquors remaining from the preparation of compounds *II* and *III* after removing compound *VIIc* in an analogous way by preparative HPLC monitored by analytical HPLC. Compound *VIII* (101 mg) had m.p. = 186—188 °C (Ref. [12] gives m.p. = 186—187 °C). Mass spectrum, *m/z*: 222 (M$^+$). ^{1}H NMR spectrum, δ: 1.34 (t, 3H, C-8—CH_2—CH_3), 2.85 (q, 2H, C-8—CH_2), 3.30 (s, 3H, N-1—CH_3), 3.50 (s, 3H, N-3—CH_3), 3.92 (s, 3H, N-7—CH_3). ^{13}C NMR spectrum, δ: 11.2 (C-8—CH_2—CH_3), 19.4 (C-8—CH_2), 27.4 (N-1—CH_3), 29.3 (N-7—CH_3), 29.4 (N-3—CH_3).

Acknowledgements. Our thanks are due to Dr. G. Bašnáková and A. Gembická (Institute of Chemistry, Slovak Academy of Sciences, Bratislava) for chromatographic measurements in the initial phase and measurement of mass spectra, respectively.

REFERENCES

1. Pfleiderer, W. and Nübel, G., *Liebigs Ann. Chem. 647*, 155 (1961).
2. Yoneda, F. and Nagamatsu, T., *J. Chem. Soc., Perkin Trans. 1 1976*, 1547.
3. Lister, J. H., *Purines*, p. 223. Wiley—Interscience, New York, 1971.
4. Rybár, A. and Antoš, K., *Collect. Czech. Chem. Commun. 35*, 1415 (1970).
5. Rybár, A., Bašnáková, G., and Staňová, A., *Chem. Papers 47*, 38 (1993).
6. Muravich-Alexandr, Kh. L., Kolesova, M. B., Pernikova, V. G., and Smirnova, N. V., *Zh. Org. Khim. 19*, 640 (1983).
7. Rybár, A. and Pfleiderer, W., *Collect. Czech. Chem. Commun. 52*, 2730 (1987).
8. Bozóová, A., Rybár, A., Alföldi, J., and Bašnáková, G., *Collect. Czech. Chem. Commun. 57*, 1314 (1992).
9. Pfleiderer, W., *Liebigs Ann. Chem. 647*, 171 (1961).
10. Pfleiderer, W. and Schündehütte, K. H., *Liebigs Ann. Chem. 612*, 158 (1958).
11. Goldner, H., Dietz, G., and Carstens, E., *Liebigs Ann. Chem. 692*, 134 (1966).
12. Huston, R. G. and Allen, W. F., *J. Am. Chem. Soc. 56*, 1793 (1934).

Translated by Z. Votický