3-ALKYL-6-METHYL-5,7-DIOXO-4,5,6,7-TETRAHYDRO-1,2,3--TRIAZOLO[4,5-*d*]PYRIMIDINES AND THEIR ALKYLATIONS

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Alkylation of 3-alkyl-6-methyl-5,7-dioxo-4,5,6,7-tetrahydro-1,2,3-triazolo[4,5-*d*]pyrimidines *I* with alkyl halides in dimethylformamide in the presence of potassium carbonate, or by analogous alkylation of sodium salts of compounds *I* afforded the respective 4-alkyl derivatives *III*, but not 5-alkyloxy-3-alkyl-6-methyl-7-oxo-6,7-dihydro-1,2,3-triazolo[4,5-*d*]pyrimidines *IV* or isomeric 1,3-dialkyl-6-methyl-5,7-dioxo-4,5,6,7-tetrahydro-1,2,3-triazolo[4,5-*d*]pyrimidinium halides *II*.

In continuation of our study on xanthine analogues we investigated the alkylation of 3-alkyl-6-methyl-5,7-dioxo-4,5,6,7-tetrahydro-1,2,3-triazolo[4,5-*d*]pyrimidines *I*, which can be regarded the 9-substituted 8-azaxanthines. Alkylation of 3-alkyltriazolo-[4,5-*d*]pyrimidines is reported[1] with 3-methyl (*Ia*) and 3-benzyl (*Ie*) derivatives; this alkylation was carried out with methyl tosylate at 125°C to give 1,3,6-trimethyl *IIa* and 1,6-dimethyl-3-benzyl-5,7-dioxo-4,5,6,7-tetrahydro-1,2,3-triazolo[4,5-*d*]pyrimidinium tosylate (*IIb*). As found, treatment of compound *I* with alkyl halide in dimethylformamide in the presence of alkali metal carbonates resulted in alkylatoni of the pyrimidine moiety and not of the triazole residue of the molecule in contrast to paper[1]. We suppose that formation of an anion in the pyrimidine moiety of the molecule took place under these alkylation conditions and consequently, alkylation occured at that part of compound *I*. Two isomeric compounds could be expected when alkylating the anion of compound *I*: 4-alkyl *III* and 5-alkoxy derivative *IV*. Aiming to find out which derivative was formed, we prepared 3,4,6-trimethyl-5,7--dioxo-4,5,6,7-tetrahydro-1,2,3-triazolo[4,5-*d*]pyrimidine (*IIIa*) and 5-methoxy-3,6--dimethyl-7-oxo-6,7-dihydro-1,2,3-triazolo[4,5-*d*]pyrimidine (*IVa*) as model substances for spectral measurements. The first (*IIIa*) was synthesized from 6-methylamino-1,3-dimethyl-2,4-(1*H*, 3*H*)-pyrimidinedione according to ref.[1] and therefore, the position of one methyl group was secured in position 4 of the triazolo[4,5-*d*]pyrimidine ring system. The second reference was prepared from 3,6-dimethyl-5,7-dioxo--4,5,6,7-tetrahydro-1,2,3-triazolo[4,5-*d*]pyrimidine (*Ia*), the enol form *V* of which

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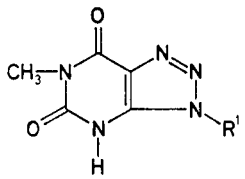
yielded 5-chloro derivative *VI* on treatment with phosphorus oxychloride in dimethylformamide. Sodium ethoxide transformed derivative *VI* into compound *IVa*.

Positions of signals in the ^1H and ^{13}C NMR spectra of the methylation product of compound *Ia* and the standard *IIIa* are the same (δ_H 3·76, δ_C 31·0), whilst signals of the 5-methoxy group in reference *IVa* appeared at δ_H 4·11 and δ_C 56·7. Position of the newly entering alkyl was also backed by the pair of absorption bands for ν(CO) in positions 7 and 5 (1 673–1 691 and 1 714–1 724 cm^{-1}, respectively) appearing in alkylation products of compound *I* and in the reference substance *IIIa* (1 673 and 1 714 cm^{-1}), whilst only one absorption band at 1 707 cm^{-1} was observed with the standard *IVa* corresponding to ν(CO) in position 7.

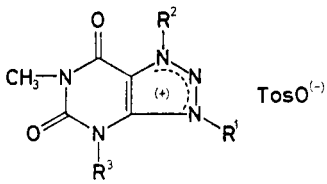
The problem with bonding an alkyl group to nitrogen in position 4 or to oxygen of the enolic hydroxyl in position 5 of triazolo[4,5-*d*]pyrimidine skeleton became even more pronounced when alkylating compounds *I* bearing bulky benzyl (*Ie*) or butyl (*Id*) groups in position 3 hindering sterically position 4. As follows from the presence of the pair of absorption bands for ν(CO) at 1 673–1 691 and 1 714 to 1 724 cm^{-1} even a great dimension of the newly entering alkyl together with the bulky substituent in the starting compound *Id* or *Ie* do not prefer formation of the enol ether of type *IV*. Evidence that the triazole ring was not alkylated brought the ^1H NMR spectra of compound *IIIa* and 1,3,4,6-tetramethyl-5,7-dioxo-4,5,6,7-tetrahydro-1,2,3-triazolo[4,5-*d*]pyrimidinium tosylate (*VII*) prepared according to ref.[1]. The methyl group singlets of compounds *IIIa* and *VII* resonated at δ 3·33 and δ 3·37, respectively (N(6)—CH_3), at 3·76 and 3·82, respectively (N(4)—CH_3), at 4·38 and 4·56, respectively (N(3)—CH_3) in addition to 4·63 (N(1)—CH_3) for compound *VII*. Signals of methyl groups in the triazole moiety are located at higher δ values.

The UV spectra (λ_{max}, nm ($\varepsilon \cdot 10^{-4}$)) revealed absorption bands formed by two peaks and a shoulder as follows: compounds *I*: 200–202 (18–20), 239–240, shoulder (4·3–4·8), 256–258 (6·9–9·4); compounds *III*: 200–206 (18·8–24·3), 243–246, shoulder (6·3–8·6), 257–261 (7·1–9·09).

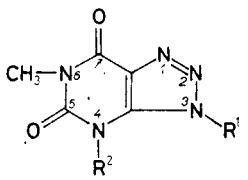
Compounds *I* were alkylated with reactive alkyl halides as methyl iodide, allyl bromide, propargyl bromide and benzyl chloride; in spite of this, only 33–69% yields were achieved with compounds *III* due to steric hindrance of position 4 by the neighbouring substituent in position 3. Another reason for the lower yields was the necessity to purify the products by recrystallization. The starting compounds *I* were obtained by a modified method described for the synthesis of *IIIa* according to refs[1,2]: 6-chloro-3-methyl-2,4-(1*H*, 3*H*)-pyrimidinedione (*VIII*) was aminated with alkylamine in excess under pressure to 6-alkylamino-3-methyl-2,4-(1*H*, 3*H*)-pyrimidinedione (*IX*). The latter was nitrosylated into position 5 with sodium nitrite and acetic acid or alternatively with propyl nitrite under acid catalysis to give the 5-nitroso derivative *X*. The intermediate *X* was hydrogenated catalytically over Raney-nickel to an unstable diamine *XI*, which, without being isolated was treated



Ia, $R^1 = CH_3$
Ib, $R^1 = C_2H_5$
Ic, $R^1 = C_3H_7$
Id, $R^1 = C_4H_9$
Ie, $R^1 = CH_2C_6H_5$



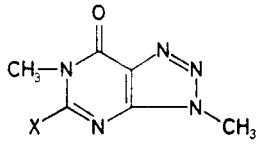
	R^1	R^2	R^3
IIa	CH_3	CH_3	H
IIb	CH_3	$CH_2C_6H_5$	H
VII	CH_3	CH_3	CH_3



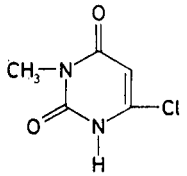
III	R^1	R^2
a	CH_3	CH_3
b	CH_3	$CH_2C_6H_5$
c	CH_3	$CH_2CH{=}CH_2$
d	CH_3	$CH_2C{\equiv}CH$
e	C_2H_5	CH_3
f	C_2H_5	$CH_2C_6H_5$

III	R^1	R^2
g	C_2H_5	$CH_2CH{=}CH_2$
h	C_2H_5	$CH_2C{\equiv}CH$
i	C_3H_7	CH_3
j	C_3H_7	$CH_2C_6H_5$
k	C_3H_7	$CH_2CH{=}CH_2$
l	C_3H_7	$CH_2C{\equiv}CH$

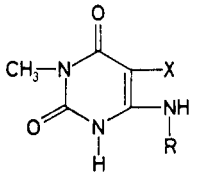
III	R^1	R^2
m	C_4H_9	CH_3
n	C_4H_9	$CH_2C_6H_5$
o	C_4H_9	$CH_2C{\equiv}CH$
p	$CH_2C_6H_5$	CH_3
q	$CH_2C_6H_5$	$CH_2C_6H_5$
r	$CH_2C_6H_5$	$CH_2CH{=}CH_2$



IVa, X = OCH_3
V, X = OH
VI, X = Cl



VIII



IX, X = H; *X*, X = NO; *XI*, X = NH_2

	R		R
a	CH_3	*d*	C_4H_9
b	C_2H_5	*e*	$CH_2C_6H_5$
c	C_3H_7		

with nitrous acid to give triazolo[4,5-*d*]pyrimidine derivative *I*. This procedure transforming the nitroso derivative *X* into compound *I* is simplier than methods

hitherto described[1,2] for compounds *Ia* and *Ie* according to which *Xa* was reacted with zinc dust and formic acid to furnish 5-formylamino derivative. The latter was hydrolyzed with methanolic hydrogen chloride to diamine hydrochloride *XIa*, which was finally treated with nitrous acid to afford compound *Ia*. Data characterizing the intermediates *IX*–*X* are listed in Table I.

Structure of compounds *I* and *III* was verified, in addition to data already mentioned, by elemental analyses, mass, ^{1}H and ^{13}C NMR spectra (Tables II and III).

EXPERIMENTAL

Melting points are uncorrected, samples for analyses were dried over phosphorus pentoxide at

TABLE I
Yields and analytical data of intermediates *IX*–*X*

Compound	Yield, % (Method)	M.p., °C	Formula (M.w.)	Calculated/Found		
				% C	% H	% N
IXa	76	303–305 300–302[a]	$C_6H_9N_3O_2$ (155·2)			
IXb	81	276–278	$C_7H_{11}N_3O_2$ (169·2)	49·70 49·51	6·55 6·59	24·84 25·03
IXc	64	245–247	$C_8H_{13}N_3O_2$ (183·2)	52·45 52·57	7·15 7·22	22·94 23·17
IXd	71	239–242 242–244[a]	$C_9H_{15}N_3O_2$ (197·2)			
IXe	70	298–300 300–302[a]	$C_{12}H_{13}N_3O_2$ (231·2)			
Xa	97(*A*) 97(*B*)	288–290 292–294[a]	$C_6H_8N_4O_3$ (184·2)			
Xb	79(*A*) 94(*B*)	237–240	$C_7H_{10}N_4O_3$ (198·2)	42·42 42·57	5·09 5·04	28·27 28·41
Xc	95(*A*)	245–248	$C_8H_{12}N_4O_3$ (212·2)	45·28 44·92	5·70 5·67	26·40 26·41
Xd	87(*A*)	237–239 238–240[a]	$C_9H_{14}N_4O_3$ (226·2)			
Xe	60(*A*)	355–360 360[a]	$C_{12}H_{12}N_4O_3$ (260·3)			

[a] Reported in ref.[4].

TABLE II

Yields and analytical data for 3-alkyl- and 3,4-dialkyl-6-methyl-2,6-dioxo-4,5,6,7-tetrahydro--1,2,3-triazolo[4,5-*d*]pyrimidines *I* and *III*

Compound	M.p., °C Yield, % (Method)	Formula (M.w.)	Calculated/Found			M^+ *m/z*
			% C	% H	% N	
Ia	312—315[a] 46	$C_6H_7N_5O_2$ (181·2)	39·78 39·73	3·89 3·58	38·66 38·90	181
Ib	294—296 43	$C_7H_9N_5O_2$ (195·2)	43·07 43·17	4·65 4·39	35·88 36·18	195
Ic	210—212 50	$C_8H_{11}N_5O_2$ (209·2)	45·90 46·05	5·30 4·98	33·48 33·75	209
Id	208—209 52	$C_9H_{13}N_5O_2$ (223·2)	48·42 48·05	5·87 5·85	31·37 31·60	223
Ie	253—254[b] 54	$C_{12}H_{11}N_5O_2$ (257·3)	56·02 55·68	4·31 4·15	27·23 27·10	257
IIIa	228—229[c] 58(*A*), 69(*B*)	$C_7H_9N_5O_2$ (195·2)	43·07 43·11	4·65 4·47	35·88 36·04	195
IIIb	180—182 48(*A*), 50(*B*)	$C_{13}H_{13}N_5O_2$ (271·3)	57·56 57·48	4·83 4·73	25·82 25·95	271
IIIc	161—162 51(*A*), 46(*B*)	$C_9H_{11}N_5O_2$ (221·2)	48·86 48·83	5·01 4·94	31·66 31·95	221
IIId	192—193 51(*A*), 62(*B*)	$C_9H_9N_5O_2$ (219·2)	49·31 49·30	4·12 4·10	31·95 32·25	219
IIIe	130—132 56(*A*)	$C_8H_{11}N_5O_2$ (209·2)	45·93 45·97	5·30 5·28	33·48 33·80	209
IIIf	190—192 68(*A*)	$C_{14}H_{15}N_5O_2$ (285·3)	58·93 58·89	5·30 5·36	24·55 24·67	285
IIIg	103—106 47(*A*)	$C_{10}H_{13}N_5O_2$ (235·2)	51·05 50·84	5·57 5·54	29·77 30·02	235
IIIh	185—187 56(*A*)	$C_{10}H_{11}N_5O_2$ (233·2)	51·49 51·32	4·75 4·71	30·03 29·91	
IIIi	109—112 68(*A*)	$C_9H_{13}N_5O_2$ (223·2)	48·42 48·49	5·87 5·81	31·37 31·62	223
IIIj	210—211 67(*A*)	$C_{15}H_{17}N_5O_2$ (299·3)	60·09 60·18	5·64 5·73	23·44 23·40	299
IIIk	117—188 39(*A*), 33(*B*)	$C_{11}H_{15}N_5O_2$ (249·3)	53·00 52·77	6·07 5·98	28·10 28·30	249

TABLE II
(*Continued*)

Compound	M.p., °C Yield, % (Method)	Formula (M.w.)	Calculated/Found			M^+ *m/z*
			% C	% H	% N	
IIIl	157–158 65(*A*), 68(*B*)	$C_{11}H_{13}N_5O_2$ (247·3)	53·44 53·61	5·30 5·38	28·32 28·57	247
IIIm	89–90 45(*A*)	$C_{10}H_{15}N_5O_2$ (237·3)	50·62 50·69	6·37 6·42	29·52 29·57	237
IIIn	149–150 43(*A*)	$C_{16}H_{19}N_5O_2$ (313·4)	61·32 60·99	6·11 5·98	22·35 22·07	313
IIIo	125–128 54(*A*)	$C_{12}H_{17}N_5O_2$ (263·3)	54·74 54·58	6·51 6·50	26·60 26·76	263
IIIp	159–162 61(*A*), 53(*B*)	$C_{13}H_{13}N_5O_2$ (271·3)	57·56 57·51	4·83 4·71	25·82 26·04	271
IIIq	192–194 56(*A*)	$C_{19}H_{17}N_5O_2$ (347·4)	65·69 65·66	4·93 5·02	20·16 19·74	347
IIIr	134–136 35(*A*)	$C_{15}H_{15}N_5O_2$ (297·3)	60·59 60·48	5·09 5·09	23·56 23·73	297

[a] Reported m.p. 296°C (ref.[1]); [b] m.p. 240–241°C (ref.[1]); [c] m.p. 222–223°C (ref.[3]).

100°C/65 Pa for 8 h. The ^1H and ^{13}C NMR spectra of hexadeuterodimethyl sulfoxide solutions measured with a Bruker AM-300 spectrometer operating at 300 and 75 MHz, respectively are relative to dimethyl sulfoxide (2·6 and 39·5 ppm, respectively, tetramethylsilane 0·00 ppm). Some signals in the ^{13}C NMR spectra were ascribed using the pulse technique DEPT and a selective decoupling. The IR spectra in KBr and the UV spectra in methanol were recorded with the respective Perkin–Elmer, model 983 and Specord M 40 (Zeiss, Jena) spectrophotometers. The mass spectra were run with a JEOL 100-D apparatus at 70 eV ionization energy. The reaction course and purity of products were monitored on thin-layer chromatography on Silufol UV_{254} (Kavalier, Votice) sheets in chloroform–methanol 9 : 1 (compounds *I* and *III*).

6-Alkylamino-3-methyl-(1*H*, 3*H*)-pyrimidine-2,6-diones *IX*

6-Chloro-3-methyl-(1*H*, 3*H*)-pyrimidine-2,6-dione[3] (*VIII*, 16·1 g, 0·10 mol) and aqueous alkylamine (30–48%; 0·80 mol for *IXa*, *IXb*; 0·60 mol for *IXc*, *IXd*; 0·50 mol for *IXe*) were heated with stirring in an autoclave at 120–130°C for 8 h (for *IXa* 2 h). The mixture was concentrated under reduced pressure, neutralized with acetic acid and the residue was crystallized from water (*IXa*–*IXc*), diluted ethanol (*IXd*), or from aqueous dimethylformamide (*IXe*).

6-Alkylamino-5-nitroso-3-methyl-(1*H*, 3*H*)-pyrimidine-2,6-diones *X*

Method A: Compound *IX* (100 mmol) was dissolved in 50% acetic acid (340 ml (compounds

TABLE III

^{1}H and ^{13}C NMR chemical shifts of compounds *I* and *III*

Compound	^{1}H NMR, (δ, ppm)			^{13}C NMR (δ_C, ppm)		
	N(3)—R^1	N(4)—R^2	N(6)—CH_3	N(3)—R^1	N(4)—R^2	N(6)—CH_3
Ia	4·07 s, 3 H (CH_3)	—	3·28 s, 3 H	33·9 (CH_3)	—	27·3
Ib	1·50 t, 3 H (CH_3) 4·48 q, 2 H (CH_2)	—	3·28 s, 3 H	14·6 (CH_3) 42·4 (CH_2)	—	27·3
Ic	0·95 t, 3 H (CH_3) 1·90 se, 2 H (CH_2) 4·40 t, 2 H (CH_2)	—	3·30 s, 3 H	10·7 (CH_3) 22·5 (CH_2) 48·5 (CH_2)	—	27·3
Id	0·95 t, 3 H (CH_3) 1·35 se, 2 H (CH_2) 1·85 qi, 2 H (CH_2) 4·95 q, 2 H (CH_2)	—	3·25 s, 3 H	13·5 (CH_3) 19·1 (CH_2) 31·0 (CH_2) 46·9 (CH_2)	—	27·4
Ie	5·72 s, 2 H (CH_2) 7·35—7·50 m, 5 H (C_6H_5)	—	3·28 s, 3 H	52·1 (CH_2) 126·2 (C_6H_5) 128·1 (C_6H_5) 129·0 (C_6H_5) 135·9 (C_6H_5)	—	27·4
IIIa	4·38 s, 3 H (CH_3)	3·76 s, 3 H (CH_3)	3·33 s, 3 H	36·7 (CH_3)	31·0 (CH_3)	28·3
IIIb	4·05 s, 3 H (CH_3)	5·50 s, 2 H (CH_2) 7·40 m, 5 H (C_6H_5)	3·38 s, 3 H	36·2 (CH_3)	46·7 (CH_2) 125·5 (C_6H_5) 127·5 (C_6H_5) 128·9 (C_6H_5) 136·2 (C_6H_5)	28·4

IIIc	4·28 s, 3 H (CH_3)	4·87 d, 2 H (CH_2) 5·20 d, 1 H (CH-*trans*) J = 17·5 Hz 5·33 d, 1 H (CH-*cis*) J = 10·5 Hz 6·18 o, 1 H (CH)	3·35 s, 3 H	36·3 (CH_3)	45·7 (CH_2) 116·3 (CH_2=) 133·1 (CH)	28·4
IIId	4·48 s, 3 H (CH_3)	3·66 t, 1 H (CH) 5·10 d, 2 H (CH_2)	3·34 s, 3 H	36·4 (CH_3)	33·7 (CH_2) 77·2 (C≡) 78·5 (CH)	28·6
IIIe	1·60 t, 3 H (CH_3) 4·68 q, 2 H (CH_2)	3·76 s, 3 H (CH_3)	3·34 s, 3 H	16·0 (CH_3) 44·8 (CH_2)	31·1 (CH_3)	28·3
IIIf	1·23 t, 3 H (CH_3) 4·40 q, 2 H (CH_2)	5·50 s, 2 H (CH_2) 7·38–7·46 m, 5 H (C_6H_5)	3·39 s, 3 H	15·3 (CH_3) 44·7 (CH_2)	47·0 (CH_2) 125·6 (C_6H_5) 127·6 (C_6H_5) 128·9 (C_6H_5) 135·7 (C_6H_5)	28·5
IIIg	1·57 t, 3 H (CH_3) 4·58 q, 2 H (CH_2)	4·83 q, 2 H (CH_2) 5·22 d, 1 H (CH-*trans*) J = 17·5 Hz 5·32 d, 1 H (CH-*cis*) J = 10·5 Hz 6·15 dd, 1 H (CH)	3·35 s, 3 H	15·9 (CH_3) 44·5 (CH_2)	45·9 (CH_2) 116·1 (CH_2=) 132·4 (CH)	28·4
IIIh	1·68 t, 3 H (CH_3) 2·61 q, 2 H (CH_2)	3·70 t, 1 H (CH) 5·18 d, 2 H (CH_2)	3·37 s, 3 H	15·8 (CH_2) 44·8 (CH_2)	34·0 (CH_2) 77·2 (C≡) 77·9 (CH)	28·1
IIIi	1·00 t, 3 H (CH_3) 1·98 se, 2 H (CH_2) 4·70 t, 2 H (CH_2)	3·72 s, 3 H (CH_3)	3·31 s, 3 H	10·9 (CH_3) 23·8 (CH_2) 50·9 (CH_2)	31·3 (CH_3)	28·4

TABLE III
(*Continued*)

Compound	^{1}H NMR (δ, ppm)			^{13}C NMR (δ_C, ppm)		
	N(3)—R^1	N(4)—R^2	N(6)—CH_3	N(3)—R–	N(4)—R^2	N(6)—CH_3
IIIj	0·75 t, 3 H (CH_3) 1·62 se, 2 H (CH_2) 4·30 t, 2 H (CH_2)	5·50 s, 2 H (CH_2) 7·45—7·53 m 5 H (C_6H_5)	3·40 s, 3 H	10·5 (CH_3) 23·4 (CH_2) 50·6 (CH_2)	47·1 (CH_2) 125·5 (C_6H_5) 127·6 (C_6H_5) 128·9 (C_6H_5) 135·7 (C_6H_5)	28·5
IIIk	1·00 t, 3 H (CH_3) 2·00 se, 2 H (CH_2) 4·50 t, 2 H (CH_2)	4·72 dd, 2 H (CH_2) 5·20 d, 1 H (CH-*trans*) J = 17·6 Hz 5·35 d, 1 H (CH-*cis*) J = 10·6 Hz 6·15 q, 1 H (CH)	3·35 s, 3 H	10·8 (CH_3) 23·7 (CH_2) 50·6 (CH_2)	46·0 (CH_2) 116·2 (CH_2=) 132·4 (CH)	28·4
IIIl	1·00 t, 3 H (CH_3) 2·08 se, 2 H (CH_2) 4·72 t, 2 H (CH_2)	3·72 t, 1 H (CH) 5·08 d, 2 H (CH_2)	3·35 s, 3 H	10·8 (CH_3) 23·5 (CH_2) 50·7 (CH_2)	34·0 (CH_2) 77·1 (C≡) 77·8 (CH)	28·4
IIIm	1·00 t, 3 H (CH_3) 1·42 se, 2 H (CH_2) 1·95 qi, 2 H (CH_2) 4·7 t, 2 H (CH_2)	3·72 s, 3 H (CH_2)	3·31 s, 3 H	13·5 (CH_3) 19·3 (CH_2) 32·4 (CH_2) 49·2 (CH_2)	31·3 (CH_3)	28·3
IIIn	0·84 t, 3 H (CH_3) 1·23 se, 2 H (CH_2) 1·60 qi, 2 H (CH_2) 4·41 t, 2 H (CH_2)	5·57 s, 2 H (CH_2) 7·45—7·53 m, 5 H (C_6H_5)	3·46 s, 3 H	13·1 (CH_3) 19·0 (CH_2) 31·9 (CH_2) 49·0 (CH_2)	47·1 (CH_2) 125·5 (C_6H_5) 127·5 (C_6H_5) 128·9 (C_6H_5) 135·6 (C_6H_5)	28·5

IIIo	1·00 t, 3 H (CH_3)	4·82 q, 2 H (CH_2)	3·35 s, 3 H	13·3 (CH_3)	42·9 (CH_2)	28·2
	1·43 se, 2 H (CH_2)	5·22 d, 1 H (CH-*trans*)		19·1 (CH_2)	116·3 (CH_2=)	
	1·95 qi, 2 H (CH_2)	J = 17·5 Hz		32·0 (CH_2)	132·4 (CH)	
	4·55 t, 2 H (CH_2)	5·33 d, 1 H (CH-*cis*)		48·7 (CH_2)		
		J = 10·5 Hz				
		6·15 m, 1 H (CH)				
IIIp	6·08 s, 2 H (CH_2)	3·56 s, 3 H (CH_3)	3·35 s, 3 H	52·1 (CH_2)	31·1 (CH_3)	28·3
	7·25 – 7·48 m,			126·2 (C_6H_5)		
	5 H (C_6H_5)			128·1 (C_6H_5)		
				129·0 (C_6H_5)		
				135·9 (C_6H_5)		
IIIq	5·61 s, 2 H (CH_2)	5·28 s, 2 H (CH_2)	3·39 s, 3 H	52·0 (CH_2)	47·3 (CH_2)	28·5
	7·02 – 7·32 m,	7·02 – 7·32 m,		126·1 (C_6H_5)	125·3 (C_6H_5)	
	5 H (C_6H_5)	5 H (C_6H_5)		128·1 (C_6H_5)	127·6 (C_6H_5)	
				129·1 (C_6H_5)	129·0 (C_6H_5)	
				135·5 (C_6H_5)	135·1 (C_6H_5)	
IIIr	5·88 s, 2 H (CH_2)	4·62 dd, 2 H (CH_2)	3·35 s, 3 H	52·0 (CH_2)	46·1 (CH_2)	28·4
	7·25 – 7·48 m,	5·18 d, 1 H (CH-*trans*)		126·3 (C_6H_5)	116·4 (CH_2=)	
	5 H (C_6H_5)	J = 17·6 Hz		128·2 (C_6H_5)	132·1 (CH)	
		5·22 d, 1 H (CH-*cis*)		129·1 (C_6H_5)		
		J = 10·5 Hz		135·6 (C_6H_5)		
		6·01 q, 1 H (CH)				

IXa—*IXd*), 1 240 ml (compound *IXe*)) and heated to 70°C; sodium nitrite (7·8 g, 112 mmol) in water (46 ml) was added dropwise to the stirred solution at 70°C within 10 min, during which the 5-nitroso derivative *X* began to separate. The mixture was cooled to 5°C, the product was filtered off, washed with water and dried at up to 40°C under reduced pressure.

Method B: Propyl nitrite (26·0 ml, 260 mmol) and a catalytical amount of hydrochloric acid (0·2 ml) were added to a stirred ethanolic (600 ml) solution of compound *IX* (65 mmol) dissolved under reflux and cooled to 35°C. During this exothermal reaction 5-nitroso derivative *X* began to separate. The stirred mixture was allowed a spontaneous cooling (c. 1 h), the product was filtered off and worked up as with method *A*.

3-Alkyl-6-methyl-2,6-dioxo-4,5,6,7-tetrahydro-1,2,3-triazolo[4,5-*d*]pyrimidines *I*

Raney-nickel (0·9 g) was added to a suspension of compound *X* (30 mmol) in distilled water (180 ml for *Xa*, *Xd*, *Xe*; 80 ml *Xb*, *Xc*) and the mixture was hydrogenated on a shaking mashine till the consumption of hydrogen ceased (about 1 340 ml at room temperature). The resulting diamino deriative was dissolved by addition of hydrochloric acid (3 ml, 30 mmol) in a nitrogen atmosphere, the catalyst was filtered off, the solution of diamine hydrochloride *XI*.HCl was cooled to 10°C and sodium nitrite (2·3 g, 33 mmol) in distilled water (20 ml) was added with stirring during 5 min. Stirring was then continued in air at 10°C for 1 h during which the product *I* separated; it was filtered off and crystallized from water (compounds *Ib*—*Id*) or dimethylformamide–ethanol (compounds *Ia*, *Ie*).

3,4-Dialkyl-6-methyl-2,6-dioxo-4,5,6,7-tetrahydro-1,2,3-triazolo[4,5-*d*]pyrimidines *III*

Method A: A mixture composed of compound *I* (1·0 mmol), water-free potassium carbonate (166 mg, 1·2 mmol), absolute dimethylformamide (6·0 ml) and alkyl halide (1·2 mmol were stirred at elevated temperature (50°C for *IIIa*, *IIIe*; 60°C for *IIIi*, *IIIm*, *IIIp*; 80°C for *IIIc*, *IIIo*; 90°C for *IIId*, *IIIg*, *IIIh*, *IIIk*, *IIIl*, *IIIp*, *IIIr*; 120°C for *IIIb*, *IIIf*, *IIIj*, *IIIn*, *IIIq*) for 1 h (*IIId*, *IIIh*), 2 h (*IIIk*, *IIIl*), 3 h (*IIIa*, *IIIf*, *IIIi*), 4 h (*IIIb*, *IIIc*, *IIIj*, *IIIm*, *IIIq*), 5 h (*IIIe*, *IIIg*, *IIIo*, *IIIp*, *IIIr*) and 6 h (*IIIn*). After the specified time, dimethylformamide was removed under reduced pressure, chloroform (30 ml) was added and the mixture was stirred for 2 h. The inorganic salts together with a part of the unreacted starting material were filtered off, the filtrate was extracted with 0·1M-NaOH (10 ml) and chloroform was distilled off under diminished pressure. The residue was crystallized from ethanol–hexane.

Method B: Compound *I* (1·0 mmol) was transformed into its sodium salt by dissolving in 1·0M ethanolic sodium hydroxide (1 ml) and ethanol (2 ml), the solvent was distilled off and the residue was dried under reduced pressure. Absolute dimethylformamide (6 ml) and alkyl halide (1·2 mmol) were added and the mixture was stirred at conditions given with method *A*, according to which also the mixture was worked up.

5-Chloro-3,6-dimethyl-7-oxo-6,7-dihydro-1,2,3-triazolo[4,5-*d*]pyrimidine *VI*

Compound *Ia* (0·40 g, 2·2 mmol), phosphorus oxychloride (8·63 ml, 93 mmol) and phosphorus pentachloride (0·65 g, 3·1 mmol) were refluxed for 6 h. Phosphorus oxychloride was distilled off and water (20 ml) was added to the residue cooled to 0°C. The product was extracted with chloroform (2 × 20 ml), the extract was washed with sodium hydrogen carbonate solution at 5°C and dried with sodium sulfate. The solvent was removed under reduced pressure and the crude product was crystallized from ethanol. Yield 0·26 g (58%), m.p. 211—213°C. For C_6H_6Cl.

.N_5O (199·6) calculated: 36·10% C, 3·03% H, 17·76% Cl, 35·00% N; found: 36·11% C, 2·99% H, 17·44% Cl, 35·29% N. Mass spectrum, *m/z*: 199 (M^+).

5-Methoxy-3,6-dimethyl-7-oxo-6,7-dihydro-1,2,3-triazolo[4,5-*d*]pyrimidine (*IVa*)

Sodium methoxide in methanol (1 ml; 1·0 mol l^{-1}) was added to a stirred suspension of compound *VI* (0·20 g, 1 mmol) in toluene (10 ml) cooled to 0°C. The mixture was left to react at room temperature for 4 h and toluene was distilled off under diminished pressure. Chloroform (15 ml) was added to the residue and sodium chloride was filtered off after a 10-minute stirring. The filtrate was concentrated to dryness in vacuo and the crude product was crystallized from ethanol. Yield 0·12 g (61%), m.p. 178–179°C. For $C_7H_9N_6O_2$ (195·2) calculated: 43·07% C, 4·65% H, 35·88% N; found: 43·17% C, 4·53% H, 36·00% N. Mass spectrum, *m/z*: 195 (M^+). IR spectrum, cm^{-1}: 1 528, 1 562 (C=N, C=C); 1 707 (C=O). ^{1}H NMR spectrum, δ: 4·17 s, 3 H (N(3)—CH_3); 4·11 s, 3 H (O—CH_3); 3·43 s, 3 H (N(6)—CH_3). ^{13}C NMR spectrum, δ: 56·7 (O—CH_3); 32·4 (N(3)—CH_3); 27·9 (N(6)—CH_3).

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