

NITROGEN BRIDGEHEAD COMPOUNDS PART 57¹. SYNTHESIS OF NEW
1-THIA-2a,5a-DIAZAACENAPHTHENES

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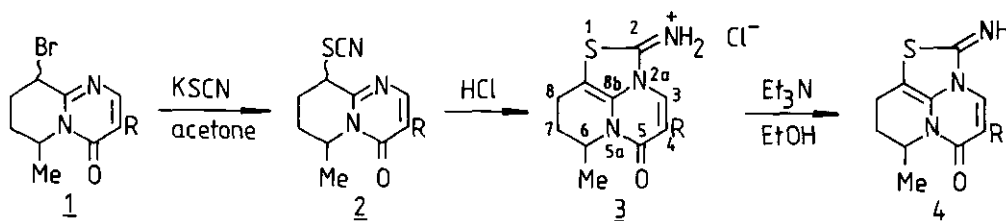
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Abstract - The first representatives of a new ring system, the
1-thia-2a,5a-diazaacenaphthenes are prepared by the reaction
of 9-bromo-6,7,8,9-tetrahydro-4H-pyrido[1,2-g]pyrimidin-4-ones
with alkali thiocyanates.

During our studies on synthesis of new annellated derivatives of biologically
active² pyrido[1,2-g]pyrimidin-4-ones recently the first derivatives of 2,3a,6a-
triazaphenalenes were prepared³. As a continuation of this work we wish to de-
scribe herein the first synthesis of 1-thia-2a,5a-diazaacenaphthenes.

For this purpose the reactivity of 9-bromo-6,7,8,9-tetrahydro-4H-pyrido[1,2-g]-
pyrimidin-4-ones⁴ was utilized. With nitrogen bases a very smooth S_N reaction⁵
and sometimes subsequent oxidation^{5a-c} have been observed. Making use of extreme
reactivity of the 9-bromo derivatives further substitutions with other nucleo-
philes, e.g. CN⁻, N₃⁻, NO₂⁻, I⁻, SH⁻, R₂NCSS⁻, and thioureas have also been ac-
complished⁶.



a) R=COOEt; b) R=CN; c) R=CONH₂; d) R=COOH

Compounds 1 (ca. 1:4 cis-trans mixture)^{4c} readily reacted with equimolar potas-
sium thiocyanate in acetone at room temperature affording 2 which without isola-
tion⁷ immediately cyclized by equimolar amount of aqueous hydrochloric acid and

the yellow hydrogen chloride salts (3)⁸ were precipitated from the solvent. The free bases of red colour (4) could be liberated from the salts (3) by triethylamine⁹. The structure of the new tricyclic ring system is unambiguously proved by correct elemental analysis, IR and NMR spectra of compounds 3 and 4. Although the fact of the ring closure is nicely indicated by the IR spectrum not containing ν_{SCN} band, ¹H and rather ¹³C NMR spectra give strong evidences for the cyclization.

In ¹H NMR spectra of compounds 3 remarkable downfield shifts ($\Delta\delta \sim 1$ ppm) of the H-3 signal occur comparing with that of the starting material (1)¹⁰. It is due to the deshielding effect the neighbouring iminium group. ¹³C NMR show three signals characteristic of the new thiazoline ring: C-2 at 164 ppm, C-8b at 127 ppm and C-8a at about 90 ppm. Deprotonation of salts 3 to compounds 4 caused a pronounced upfield shift on C-2, C-4, C-8a, and C-8b.

¹ H NMR Chemical shifts		JEOL FX-100 solvent DMSO-d ₆ δ (TMS) = 0 ppm							
Comp.	6-Me	H-6	CH ₂ -7,8		H-3	CH ₃	CH ₂ O	NH(HCl)	
<u>3</u> a	1.14d	4.74m	1.7-2.2m	2.4-2.8m	9.31e	1.32t	4.27q	10.30	13.30
<u>4</u> a*	1.25d	4.85m	1.95m	2.35m	8.55s	1.35t	4.25q		
<u>3</u> b	1.15d	4.72m	1.6-2.2m	2.4-2.9m	9.42s			5.85	
<u>4</u> b	1.12d	4.61m	1.6-2.1m	2.2-2.5m	8.57s			9.70	
<u>3</u> c	1.10d	4.82m	1.7-2.3m	2.6-2.8m	9.10s			7.87	8.42
<u>4</u> c	1.14d	4.70m	1.7-2.2m	2.3-2.8m	8.59s			9.52	

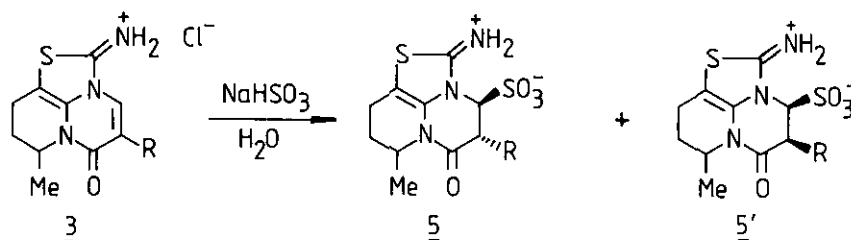
* in CDCl₃

¹³ C NMR Chemical shifts		JEOL FX-100 solvent DMSO-d ₆											
Comp.	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-8a	C-8b	Me	R		
<u>3</u> a	164.8	136.9	111.5	152.3	45.4	25.5	16.3	88.9	127.0	16.1	14.1	61.4	161.6
<u>4</u> a*	156.4	138.1	104.3	154.9	44.8	26.2	16.9	81.8	124.9	16.4	14.3	60.9	162.6
<u>3</u> b	164.3	141.3	95.6	151.7	46.1	25.2	16.4	91.0	126.1	16.2		112.1	
<u>4</u> b	152.8 ⁺	141.0	87.7	154.0 ⁺	45.0	25.1	16.3	83.9	123.4	16.0		114.5	
<u>4</u> c	154.2 ⁺	136.8	104.8	157.8 ⁺	44.7	25.4	16.2	82.1	124.5	16.0		162.8	

* in CDCl₃; + tentative assignment

We have investigated some nucleophilic reactions of the new tricyclic salts (3)

but in most cases only anion exchange (SCN^- , N_3^- , I^-) or the liberation of the free bases (4) (CN^- , OCN^-) have been observed. With HSO_3^- anion, however, Michael addition on the C-3 and C-4 double bond took place resulting in a fairly stable betaines (5+5')¹¹.



The adducts are in all cases 1:1 mixtures of the cis (5') and trans (5) isomers. As both isomers have the SO_3^- group in pseudoaxial position owing to the peri effect of the neighbouring iminium group, the position of the R group is different. This is supported by the multiplicity and coupling constant of the H-3 and H-4 protons ($^3J_{3,4} \approx 1.0\text{Hz}$). The isomeric ratio can be determined by the intensity of the H-3 signals.

Recently we have described¹² a similar sensitivity towards nucleophiles in the case of the 2,3a,6a-triazaphenalenium salts where the site of the nucleophilic attack was the same carbon atom of the pyrimidine moiety as with compounds 3.

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7. Only compound 2c could be isolated in pure form owing to its very poor solubility in acetone. Mp 190-192 °C, ¹H NMR (DMSO-d₆): Me 1.33d, H-6 4.56m, H-9 5.1-5.3m; H-2 8.63s; NH₂ 7.80 and 8.40 ppm broad.
8. 3a: Yield 71%, mp 210 °C; 3b: Yield 57%, mp 244-245 °C; 3c: Yield: 75%, mp 243-245 °C; 3d: Yield 69%, mp 203-204 °C.
9. Reaction was carried out in methanol with a slight excess of triethylamine. 4a: mp 144-145 °C (EtOH); 4b: mp 166-168 °C (EtOH); 4c: mp 203-205 °C (EtOH).
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11. To the yellow suspension of 3 in water excess of solid NaHSO₃ was added at 25 °C and stirred while the mixture became white. The precipitated crystals were filtered off, and washed with water. 5a and 5a': mp 196-198 °C; characteristic NMR data (DMSO-d₆): H-3 5.67d (³J=1.0Hz) and 5.71d (³J=1.2Hz); C-3 66.5 (¹J=157.0Hz) and 66.7 (¹J=157.0Hz); C-4 48.2 (¹J=141.6Hz) and 48.9 (¹J=141.6Hz). 5b and 5b': mp 250 °C; in solution it decomposed to 4b, 5c and 5c': mp 198-200 °C; H-3 5.44d (³J=1.0Hz) and 5.48d (³J=1.0Hz). 5d and 5d': mp 250 °C; H-3 5.24d (³J=1.0Hz), and 5.30d (³J=1.0Hz).
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