

NITROGEN BRIDGEHEAD COMPOUNDS PART 21<sup>1</sup>. PREPARATION OF NEW QUATERNARY  
2,3a,6a-TRIAZAPHENALENIUM SALTS

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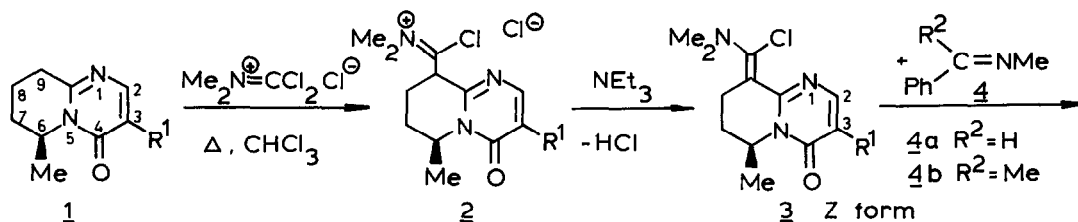
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**Summary:** The first representatives of a new ring system, the 2,3a,6a-triazaphenalenium quaternary salts are prepared by the cycloaddition of tetrahydro-4H-pyrido[1,2-a]pyrimidin-4-ones containing an  $\alpha$ -chloroamine moiety with azomethines.

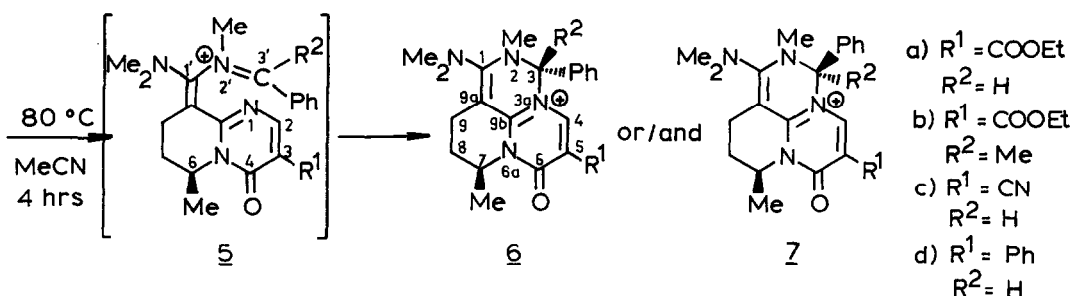
Earlier we have reported<sup>2</sup> that 6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidin-4-ones (1) contain an active methylene group in position 9. Numerous electrophilic reactions have been accomplished on this site of the molecule, e.g. halogenation<sup>3</sup>, diazonium coupling<sup>4</sup>, acylation with isocyanates<sup>5</sup> and reactive iminium chlorides<sup>6</sup>. From pharmacological considerations we aimed to bring about a new ring between the N-1 and C-9 atoms.

For this purpose compounds 2, derived from 1 and phosgeneiminium-chloride<sup>6</sup>, proved to be convenient starting materials. Compounds 2 as amide chlorides generally are versatile starting materials for different reactions e.g. by loss of HCl they can smoothly be transformed into  $\alpha$ -chloroamines 3 which are expected to take part in cycloaddition reactions. Similar cycloadditions of  $\alpha$ -chloroamines were thoroughly investigated by Viehe and his co-workers<sup>7</sup> in the last decade. They observed the cycloadditions of simple  $\alpha$ -chloroamines with olefines, acetylenes, nitriles and azomethines.

These results tempted us to accomplish similar cycloaddition reactions with heterocyclic enamines of type 3. We failed to carry out cyclisation reactions with C=C double bonds but our attempts were successful in the case of aldimines and ketimines. It has turned out that the cyclisation of  $\alpha$ -chloroamines 3 with the imines 4 takes place under mild conditions, at room temperature in solvents such as  $\text{CHCl}_3$  or MeCN. All of the cycloaddition products obtained in MeCN at 80°C are well-defined salt-like compounds of pale yellow colour, soluble in water and polar organic solvents.



a)  $R^1 = \text{COOEt}$ , b)  $R^1 = \text{CN}$ , c)  $R^1 = \text{Ph}$



For the structure of the products a bicyclic form 5 and tricyclic forms 6 and 7 can be considered. To prove the structure  $^1\text{H}$ ,  $^{13}\text{C}$  nmr studies and X-ray investigations were carried out.  $^1\text{H}$  nmr was not sufficient to distinguish between the structures, as for instance in the case of the product obtained from 3a and 4a the singlets appearing at 8.34 and 9.72 ppm can be assigned to H-3 and H-4 protons  $^{8a}$  of the tricyclic products (6a or 7a), but also to H-2 and H-3' protons  $^{8b}$  of compound 5a. Proof for the cyclised product was afforded by the  $^{13}\text{C}$  nmr where the signal of C-3 appears at 75 ppm affirming its  $\text{sp}^3$  character<sup>9</sup>. In the cyclisation reaction a second asymmetric centre is formed in position 3 thus diastereomers 6 and 7 are to be expected. The products obtained under the above reaction conditions seemed to consist of one isomer according to  $^1\text{H}$  and  $^{13}\text{C}$  nmr, but these spectra did not allow configurational distinction. X-ray investigation of the product of 3b and 4a showed the trans structure<sup>10</sup>, 6c (see Fig.).

$^1\text{H}$  nmr Chemical shifts, (intensity) ppm JEOL FX-100

solvent  $\text{CDCl}_3$   $\delta(\text{TMS}) = 0$

Com- pounds	Me-7	H-7	NMe <sub>2</sub>	NMe	Ar-3	H-3 or Me	H-4	COOEt or Ph-5	y[%]	mp[°C]
<u>6a</u>	1.28d (3H)	5.0m (1H)	3.19s (6H)	3.80s (3H)	7.2m (5H)	8.34s (1H)	9.73s (1H)	4.30q (2H) 1.38t (3H)	93	233
<u>7a</u> *	1.18d (3H)	5.0m (1H)	3.13s (6H)	3.76s (3H)	7.2m (5H)	8.29s (1H)	9.78s (1H)	4.29q (2H) 1.38t (3H)	not isolated	
<u>6b</u>	1.30d (3H)	5.0m (1H)	3.37, 3.32s (6H)	3.47s (3H)	7.2m (5H)	2.37s (3H)	8.64s (1H)	4.36q (2H) 1.40t (3H)	91	207
<u>6c</u>	1.33d (3H)	4.9m (1H)	3.26s (6H)	3.64s (3H)	7.3m (5H)	7.56s (1H)	9.35s (1H)	-	93	252
<u>6d</u>	1.30d (3H)	4.9m (1H)	3.08s (6H)	3.70s (3H)	7.2m (5H)	8.07s (1H)	9.12s (1H)	7.4m (5H)	86	170

$^{13}\text{C}$  nmr Chemical shifts, JEOL FX-100 solvent= $\text{CDCl}_3$   $\delta(\text{TMS})=0$  ppm

Com- pounds	C-1	NMe <sub>2</sub>	Me-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-9a	C-9b
<u>6a</u>	148.9	42.6	42.6	75.4	148.9	107.0	161.7	47.0	25.7	18.9	86.2	154.9
<u>7a</u> *	150.4	42.9	42.9	75.7	148.2	107.8	161.7	48.2	24.8	20.4	86.1	155.1

\*signals assigned by adding 6a to the solution containing 6a and 7a in a ratio 1:1

In order to obtain some information on the mechanism of the cyclisation we have accomplished the reaction of 3a and 4a in nmr tube at 25°C. The expected pathway is the quaternisation of the imine followed by the nucleophilic attack of the ring nitrogen atom on the iminium carbon but a concerted mechanism could not be excluded either. We have established that the tricyclic compound forms stepwise: the first step leads very quickly to the quaternised molecule 5a which than cyclises to 6a and 7a with a half-period of about one hour (see Table below)

Characteristic  $^1\text{H}$  nmr signals\* of the reaction mixture of 3a and 4a in  $\text{CDCl}_3$  at 25°C at different times  
JEOL FX-100

Compds Time(min)	<u>3a</u>		<u>4a</u>		<u>5a</u>				<u>6a</u> and <u>7a</u>			
	H-2	NMe <sub>2</sub>	CH	NMe	H-3'	H-2	NMe	NMe <sub>2</sub>	H-3	H-4	NMe	NMe <sub>2</sub>
0	8.48	3.03	8.13	3.42	-	-	-	-	-	-	-	-
1	-	-	-	-	8.65	8.37	3.52	2.91	-	-	-	-
100**	-	-	-	-	8.67	8.53	3.52	2.92	8.25	9.73	3.60	3.19
									8.30	9.81	3.71	3.24

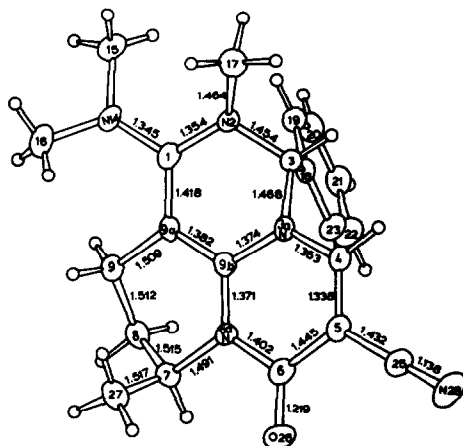
\*all signals are singlets

\*\*the ratio of 5a, 6a and 7a is cca 0.5:1:1

This investigation gave also an insight into the stereochemistry of the process. Under such conditions diastereomers 6a and 7a were formed in 1:1 ratio. When, however, this reaction mixture was heated at reflux temperature for 16 hour in acetonitrile, only diastereomer 6a was detected indicating that 7a is the kinetic while 6a is the thermodynamic product.

#### References and notes

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- 2 G.Náray-Szabó, I.Hermecz and Z.Mészáros: J.C.S.Perkin I. 1974, 1753.
- 3 I.Hermecz, T.Breining, Z.Mészáros, G.Tóth and I.Bitter: Heterocycles 14, 1953 (1980)
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- 5 I.Bitter, I.Hermecz, G.Tóth, P.Dvortsák, Z.Bende and Z.Mészáros: Tetrahedron Letters 1979, 5033.



ORTEP diagram of 6c cation with relevant bond lengths, max. e.s.d.: 0.004 Å

- 6 I.Hermecz, I.Bitter, A.Horváth, G.Tóth and Z.Mészáros: *ibid* 1979, 2557.
- 7 Advances in Organic Chemistry Vol. 9. L.Ghosez and J.Marchand-Brynaert, "Iminium Salts in Organic Chemistry" Part 1, H.Böhme and H.G.Viehe, Eds. Interscience, New York, 1976, p.421.
- 8a The H-2 signals in 1<sup>11</sup> and 3 appear between 8.2 and 8.5 ppm. We have earlier observed that this signal undergoes a downfield shift of about 1 ppm when ring annellation takes place on the N-1 atom.
- 8b On the other hand the CH-signals of simple aldiminium salts appear around 9 ppm<sup>12</sup>. The time-dependent <sup>1</sup>H nmr investigations showed later that the H-3' signal of 5a appears at higher field (at 8.66±0.01 ppm).
- 9 G.A.Olah and D.J.Donovan: *J.Org.Chem.* 43, 862 (1978).
- 10 The X-ray analysis of 6c. Crystal data: C<sub>21</sub>H<sub>24</sub>ClN<sub>5</sub>O.C<sub>2</sub>H<sub>5</sub>OH, Fwt: 443.932. Pale yellow crystals of space group P $\bar{1}$ (No2), a=10.627(2), b=11.233(3), c=11.744(2) Å,  $\alpha$ =111.40(3),  $\beta$ =110.54(3),  $\gamma$ =97.86(3)<sup>0</sup>, Z=2, (Mo-K $\alpha$  radiation,  $\lambda$ =0.71073 Å), 4089 reflexions were collected on an ENRAF-NONIUS CAD4 diffractometer. The structure has been established by direct methods and refined by anisotropic full matrix least-squares method to a final R=0.06 for 3184 reflections [ $I > \sigma(I)$ ]. Hydrogen atoms were located in difference map. All calculations were performed on a PDP 11/34 (64k) minicomputer using the E.N. SDP program package. Relevant data are deposited (Tetrahedron Letters 1978, 3081).
- 11 G.Tóth, I.Hermecz and Z.Mészáros: *J.Heterocyclic Chem.* 16, 1181 (1979).
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