NITROGEN BRIDGEHEAD COMPOUNDS PART 23[1]. RING TRANSFORMATION
OF THE 2,3a,6a-TRIAZAPHENALENIUM CHLORIDES

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Abstract: The 2,3a,6a-triazaphenalenium salts (1,2) undergo degenerated
ring transformation in basic media resulting in stable mesomeric be-
taines (4,5).

In our previous paper we reported the preparation[2] of the novel ring system, the
2,3a,6a-triazaphenalenium chloride (1) and their reaction with nucleophiles[1]. We
have established that a Michael-type addition takes place with HSO_3^- and CN^- anions
affording the novel tricyclic mesomeric betaines 6,7.
In our further experiments with aqueous alkali hydroxide, however, we have obtained
a product which failed to show the usual behaviour of pseudobases or Michael ad-
ducts. These materials being insoluble in water precipitate instantly from aqueous
solution of 1 with concentrated alkali hydroxide or within a few hours from ethanol ,
aqueous acetonitrile solution when refluxing with triethylamine or potassium carbo-
nate. Their ^{1}H and ^{13}C nmr spectra show the starting triazaphenalenium-skeleton
was retained but the substituents of the B ring changed: the 5-carboxylic acid
moiety of 1 seemed to be reduced to a formyl group and the C4 olefinic carbon atom
be oxidized to an oxo (imino) group. These radical changes are rather
difficult to explain by an intramolecular oxido-reduction step and led us to the
conclusion that they must be accompanied with ring opening and reclosure result-
ing in the same triazaphenalenium-skeleton. Although these structures for the pro-
ducts[4] 4a and 4b were affirmed by X-ray crystallography[5] the process itself re-
mained unknown as we have failed to trap àny intermediate of 4. A possible path-
way for the formation of 4 is given in Scheme 1. The initial step of the ring
transformation is suggested by the reaction of CN^- and HSO_3^- ions[1]: we have assumed
that the OH^- anion adds in a similar manner on the C4-C5 double bond. After de-
protonation, 3 undergoes ring opening followed by rotation and the ester moiety
can acylate the imine nitrogen atom affording the stable mesomeric betaine (4).
The same reaction course must be accepted for the transformation of the carbo-
nitrile derivative, too, although the reclosure of the B ring in basic media seems
to be a quite unique step. Quantum chemical calculations also predicted the nucleo-
philic attack at C4. Namely, there are six sp^2-hybridized carbon atoms in the mole-
cule C1, C4, C5, C6, C9a and C9b which are, in principle, accessible for an attack.
The minimum of the nucleophilic molecular potential map, as calculated from bond
increments[6,7], is located near C9b. Another factor which has to be taken into

account is the energy change during a reaction approximated by the sum of rigid molecule interaction and geometry distortion terms. The latter would be very high for C9b which is located in a triple bridgehead position[8,9]. Therefore, nucleophilic attack occurs at C4 where the interaction potential is only slightly higher

R = CN ; COOEt
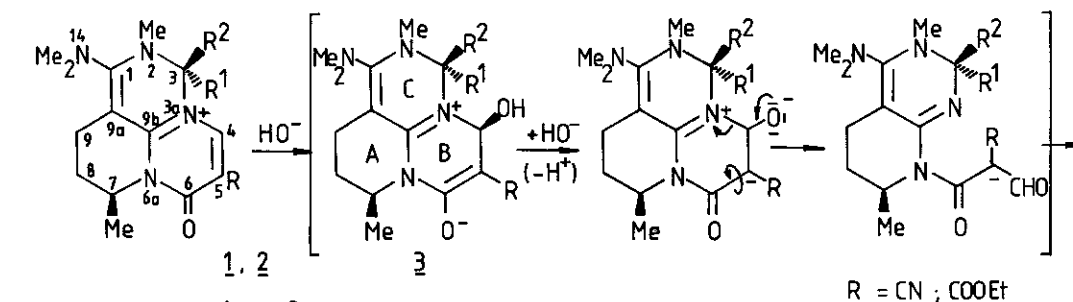
	R	R[1]	R[2]	Ref.
1a	COOEt	iPr	H	3
1b	CN	Ph	H	2
1c	COOEt	Ph	H	2
2c	COOEt	H	Ph	2

Scheme 1.

	R[1]	R[2]	X
4a	iPr	H	O
4b	Ph	H	NH
4c	Ph	H	O
5c	H	Ph	O
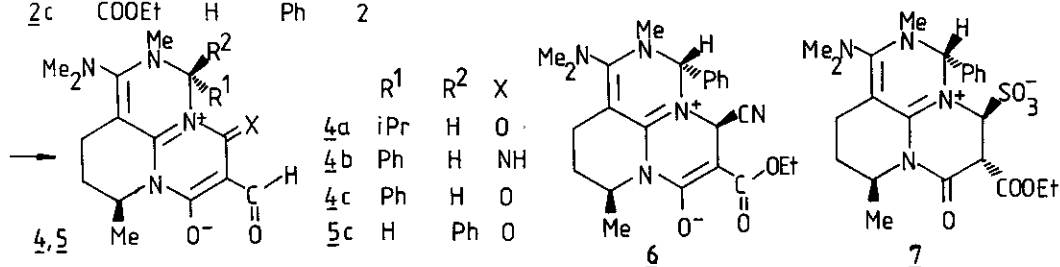
than at C9b. In order to estimate the direction of the attack, potentials at a distance of 1.70 Å from C4 above (Fig. 1) and below the ring system were calculated. The numerical values (-165, -55 kJ/mol, respectively) favor an attack from the opposite side of the phenyl group as in the case of 6 and 7[2].

Mesomeric betaines 4 show remarkable stability attributable to the extensive delocalisation of the positive and negative charges, the former among the N14, C1, N2 , C9b, N3a, N6a and the latter among the X24, C5, O28, O26 atoms (Fig. 2). These delocalisations can well be demonstrated by the respective bond lengths (Fig. 2) and bond angles: all carbon atoms taking part in the delocalization in 4a and 4b have pure sp[2] character as the sum of the angles around them is 360°±0.1. A further evidence of delocalization is the distortion of the C5-C6=O26 and C5-C25=O28 bond angles varying between 126-129°.

Earlier[2] we reported that 2c isomerised into 1c upon heating, via ring opening and reclosure between the atoms C3 and N3a. The potential barrier of this reaction measured recently by ^{1}H nmr was 123 kJ/mol. A mixture of 1c and 2c was transformed into 4c and 5c with the same isomer ratio which could not be changed by heating.

^{1}H nmr Chemical shifts JEOL-FX-100 solvent=CDCl$_3$ TMS = 0 ppm

Compd	H-7	Me-7	NMe$_2$	Me-2	iPr(Ar)-3	H-3	CH$_2$-8,9	CHO	NH
4a	5.06m	1.23d	3.08s	3.08s	1.00d;0.81d	5.68d	1.8-2.7m	10.05s	–
4b	5.06m	1.23d	3.08s	3.28s	7.2m	7.70s	1.8-2.7m	10.35s	9.68s
4c	5.08m	1.26d	3.13s	3.27s	6.9m	7.45s	1.6-2.9m	10.18s	–

^{13}C nmr Chemical shifts JEOL-FX-100 solvent=CDCl$_3$ TMS = 0 ppm

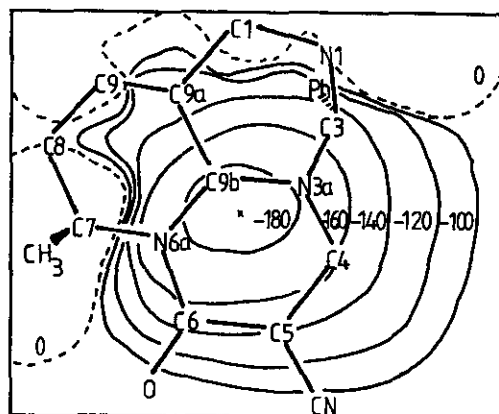|	Me-6	NMe$_2$	Me-2	C3	C5	C7	C8	C9	C9a	CHO	C1[+]	C4[+]	C6[+]	C9b[+]
4a	15.4	40.9	41.3	71.5	97.0	44.2	18.3	25.8	82.1	185.8	149.7	159.6	160.0	159.3
4b	16.3	41.5	41.2	67.3	94.9	44.6	18.3	26.5	84.8	186.9	151.6	154.8	160.9	152.0
4c	16.1	41.7	41.5	67.3	97.4	44.9	18.9	26.2	84.4	186.8	160.7	160.3	161.0	151.0

[+]interchangeable

Fig. 1. Nucleophilic molecular potential map for 1b in a plane
1.70 Å above the pyrimidine ring B (in kJ/mol). The
phenyl group at C3 is directed below the molecular plane.

Among tetrahydropyrido[1,2-a]pyrimidines two types of ring transformation were ob-
served earlier with basic catalysts effecting in both cases the B ring and yielding
1,8-naphthyridines[10] and modified pyrido[1,2-a]pyrimidines[11], respectively.
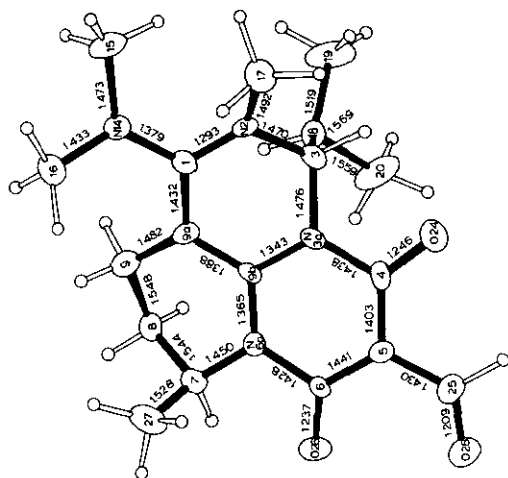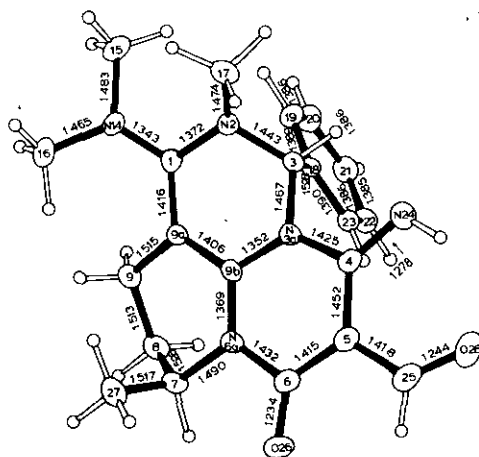
<center>I. Compound <u>4</u>a   II. Compound <u>4</u>b</center>

Fig.2. ORTEP diagram of <u>4</u>a /I/ and <u>4</u>b /II/ showing atomic numbering and bond distances /Å/; E.s.d. 's are in the range of 0.004-0.008 Å.

REFERENCES AND NOTES

1. Part 22. I.Bitter, B.Pete, I.Hermecz, K.Simon, G.Tóth, Z.Mészáros: <u>Heterocyles</u>, 1983, <u>2o</u>, 579 and Ring Transformation Part 7, Part 6: I.Hermecz and Z.Mészáros, <u>ibid.</u>, 1979, <u>12</u>, 14o7.

2. I.Bitter, B.Pete, I.Hermecz, G.Tóth, K.Simon, M. Czugler, Z.Mészáros: <u>Tetrahedron Letters</u>, 1982, <u>23</u>, 2891.

3. <u>1</u>a was obtained from ethyl 9-[(dimethylamino) chloromethylene]-6-methyl-6,7,8,9-tetrahydro-4-oxo-4H-pyrido[1,2-a]pyrimidine-3-carboxylate with $MeN=CHCH(Me)_2$ as described earlier[2]. Yield, 7o%, mp 114-118°C (MeCOEt).

4. <u>4</u>a: Yield, 68%, mp 232°C (C_6H_6), UV(EtOH) λ_{max} 368 nm (lgξ4.48) , 272(3.75) , 22o (4.14); <u>4</u>b: yield, 86%, mp 236°C (EtOH), UV(EtOH) λ_{max} 366 nm (lgξ4.52), 266 (4.0), 234(4.43); <u>4</u>c: Yield, 72%, mp 29o°C (EtOH).

5. X-ray analyses of <u>4</u>a and <u>4</u>b. <u>4</u>a Emp. formula $C_{18}H_{26}N_4O_3 \cdot C_6H_6$ a = 13.650(2) Å, b= 11.841 (4) , c=14,654(2) Å, β= 99,76 (2)°; space group $P2_1/n$; Z = 4, Radiation Mo-K$_\alpha$ λ=0.71o7 Å; 1379 reflections $(I \gtrless 2\xi(I))$; R index 0.o82. <u>4</u>b Emp. formula $C_{21}H_{25}N_5O_2$; a = 8.5o3 (1) Å, b = 13.238 (1), c = 17.257(2) Å, space group $P2_12_12_1$; z = 4; Radiation Cu-K$_\alpha$ λ = 1.5418 Å; 217o $(I \gtrless 3\xi(I))$ reflexions; R index 0.045. Data were collected on an ENRAF NONIUS CAD4 diffractometer, all calculations were performed on a PDP 11/34 (64k) minicomputer using EN. SDP program package. Relevant data are available from the authors on request.

6. G.Náray-Szabó, A.Grofcsik, K.Kósa, M.Kubinyi, A.Martin: <u>J.Comput.Chem.</u> 1981, <u>2</u>, 58.

7. G.Náray-Szabó, <u>Acta Phys.Acad.Sci.Hung.</u>, 1981, <u>51</u>, 65.

8. H.Nakatsuji, T. Kuwata, A.Yoshida, <u>J.Am.Chem.Soc.</u>, 1973, <u>95</u>, 6894.

9. O.Neunhoffer and H.Haasse, <u>Chem.Ber.</u> 1958 <u>91</u>, 1o81.

1o. I.Hermecz and Z.Mészáros, <u>Heterocycles,</u> 1979, <u>12</u>, 14o7.

11. I.Hermecz, I.Engler, Z.Mészáros, G.Tóth: <u>Tetrahedron Letters</u>, 1979, 1337.