FORMATION OF A STRAINED TRIAZAPENTALENOINDENE SKELETON VIA THE REARRANGEMENT OF 2,3-DIHYDRO-7-NITRO-1*H*-IMIDAZO[2,1-*a*]-PHTHALAZIN-4-IUM-6-OLATE EFFECTED BY DICHLOROACETIC ANHYDRIDE

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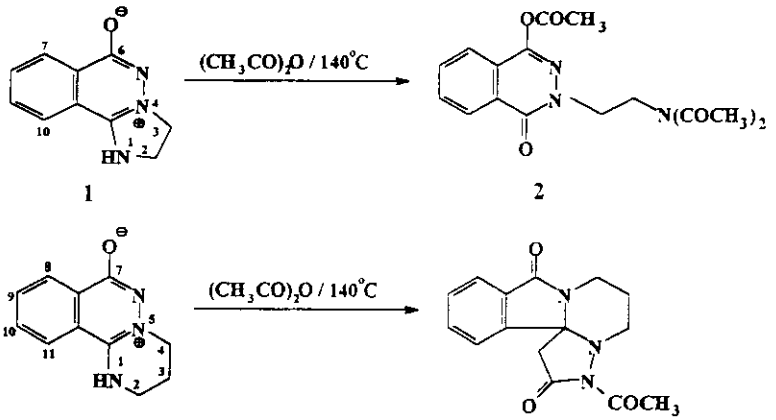
Abstract- On treatment with dichloroacetic anhydride 2,3-dihydro-7-nitro-1*H*-imidazo[2,1-*a*]phthalazin-4-ium-6-olate (**5**) underwent a backbone rearrangement leading to isoindole derivative (**12**), which represents a new strained ring system with three condensed five-membered heterocycles. The structure of its stable 3-deacylated form, 3,3a,5a-triaza-1,1-dichloro-1,2,3,3a,4,5,6,6a-octahydro-7-nitropentaleno[3a,3-*a*]-indene-2,6-dione (**13**) was evidenced by ir, ms, nmr, and X-ray methods.

Körmendy *et al.* have previously detected a highly remarkable difference between the reactivities of 2,3-dihydro-1*H*-imidazo[2,1-*a*]phthalazin-4-ium-6-olate (**1**) and its ring homologue, 1,2,3,4-tetrahydropyrimido[2,1-*a*]phthalazin-5-ium-7-olate (**3**) toward refluxing acetic anhydride [1,2] Under these vigorous acetylation conditions the imidazo derivative undergoes a ring cleavage resulting 2-(2-diacetylaminoethyl)-4-acetoxyphthalazin-1(2*H*)-one (**2**),[1] while the pyrimido homologue yields an interesting product with a fundamentally changed ring system (**4**)[2] (Scheme 1).

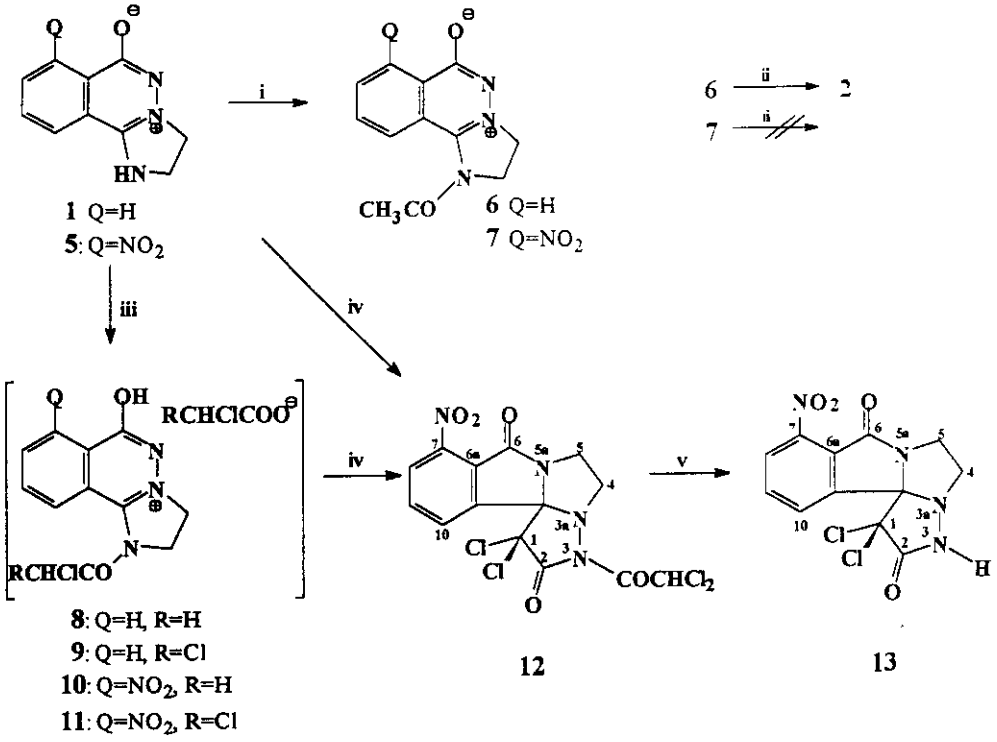


1 2

3 4

Scheme 1.

As a part of a systematic mechanistic study we aimed to examine whether the same type of transformation can be realized also in the case of imidazophthalazinium-olates, e.g. by applying more powerful acylating agents, such as mono- and dichloroacetic anhydrides. The chloroacetate ions generated in the course of the acylation are considered to be less capable of bringing about Bamberger-like ring fission (see in Ref. 1) finally resulting in diacylaminoethyl compounds analogous to **2**. Furthermore, it has already been established that 8-nitro substitution of the pyrimido-phthalazinium-olates facilitates the ring transformation, whereas 9,10-dimethoxy substitution exerts considerable retardation on it.[2] Therefore the reactions of **1** and its 7-nitro derivative (**5**)[3] were studied in more detail with acetic, mono- and dichloroacetic anhydrides (Scheme 2), and some preliminary results are reported in this paper.



Scheme 2. *i)* $(CH_3CO)_2O$ at 140°C for 0.5-1 h *ii)* $(CH_3CO)_2O$ at 140°C for 4 h *iii)* $(CH_2ClCO)_2O$ or $(Cl_2CHCO)_2O$ at 140°C for 10 min *iv)* $(Cl_2CHCO)_2O$ at 140°C for 4 h *v)* Recrystallization from EtOAc

On a shorter period of treatment (0.5-1 h) with acetic anhydride, refluxing at 140°C the precursors (**1** and **5**) converted into poorly soluble salt-like monoacetyl products isolated in 32-60% yields. Their ir spectra exclude both *O*- and *N*(5)-acetylation,[4,5] containing neither carbonyl band around 1760 cm^{-1} nor any coupled bands around 1700 cm^{-1} characteristic for enolester and imide moieties, respectively. Instead, the presence of single amide-I band and the absence of N-H vibrational band above 3000 cm^{-1} strongly suggest zwitterionic structure for these salt-like compounds

(**6** and **7**).[5] *N*(1)-Acetylation is also supported by ^{1}H-nmr spectra:[5] (i) the significant downfield shift of the A_2B_2 methylene signals refers to the electron deficiency of the positively charged imidazolinium ring; (ii) in the course of DNOE experiments, when the singlet due to the methyl group is irradiated, the H-10 signal becomes more intensive.

Empolying chloroacetic anhydrides as reagents, complete *N*(1)-acylation of the precursors could again be detected, even after 10 minutes of treatment at 140°C. Although the highly moisture-sensitive products (**8-11**) were not isolated, their structure can be regarded as proved on the basis of directly recorded ^{1}H-nmr spectra (solvent: DMSO-d_6 dried by the small amount of anhydride left after evaporation of the reaction mixture) : (i) the very characteristic downfield shift of the H-10 signal (9.0-9.1 ppm, dd, J_{ortho} = 7.2-7.9 Hz, J_{meta} = 1.9-2.9 Hz) can be attributed to the deshielding anisotropic effect of the nearby carbonyl oxygen;[6,7] (ii) the high chemical shift range of the A_2B_2 methylene signals (4.5-4.8 ppm) provides additional evidence of *N*(1)-acylation.[8]

Heating the *N*(1)-acyl derivatives (**6-11**) in the corresponding anhydride at 140°C for 4 hours, four (**7-10**) of them practically remained unchanged, **6** got converted into **2** with 22% yield, while **11** - quite surprisingly - got transformed into **12**, a novel tetracyclic derivative[9] which is closely related to compound (**4**). However, during recrystallization from ethyl acetate probably contaminated with some ethanol, **12** suffered a fast deacylation affording 3,3a,5a-triaza-1,1-dichloro-1,2,3,3a,4,5,6,6a-octahydro-7-nitropentaleno[3a,3-*a*]indene-2,6-dione (**13**), a stable representative of the new heterocyclic ring system.[10] The ^{13}C-nmr spectra taken of **12** and **13** clearly show that recrystallization did not result any change in the backbone.[9,10] By the procedure described above **13** could be obtained from the starting compound (**5**) with 35% overall yield. The complicated strongly coupled multiplets of 4H intensity in the range 3.3-4.2 ppm of the ^{1}H-nmr spectrum indicated the presence of a rigid ring in the product (**13**) with two methylene groups carrying non-equivalent geminal hydrogens. Additionally, the relatively high amide-I ir frequencies of the lactam moieties reflected considerable internal strain of the whole skeleton with condensed five-membered rings. Nevertheless, no unequivocal evidence for the structure of **13** could be derived from ir, ms, ^{1}H- and ^{13}C-nmr spectra (data are listed in note 10). Therefore we resorted to single crystal X-ray diffraction measurement,[12] which verified the assumed triazapentalenoindene skeleton of **13** (Figure 1). It is worth to point out that in spite of the results of the modelling studies which predicted large internal strain, this heterocycle related to some extent to indole alkaloides can also form. The detailed mechanistic study of this ring transformation will be the subject of a separate paper.

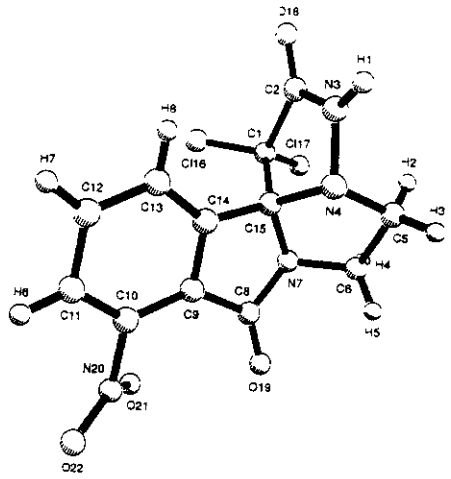


Figure 1. Structure and solid-state conformation of compound **13**

ACKNOWLEDGEMENTS

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2. K. Körmendy, A. Kálmán, T. Koritsánszky, I. Kövesdi, P. Sohár, and F. Ruff, *Acta Chim. Hung.*, 1986, **123**, 15.
3. Starting from 3-nitrophthalic anhydride, **5** was prepared by the reaction sequence analogous to that reported for preparation of its ring homologue, 1,2,3,4-tetrahydro-8-nitropyrimido[2,1-*a*]phthalazin-5-ium-7-olate (see in Ref. 2). Description of **5**: mp > 360°C; ms $M^{+\cdot}$ 232 ; ir(cm^{-1}) ν_{N-H} 3200-2100, $\nu_{C=N}$ 1605 and 1580, ν_{NO_2} 1550 and 1370; ^{1}H-nmr -$(CH_2)_2$- 4.11 and 4.48 (A_2B_2, J = 9.8 Hz, 4H), ArH 8.0-8.3 (m, 3H), N-H 10.68 (s, 1H).
4. The structure of **6** was incorrectly assigned in Ref. 1 as 5-acetyl-2,3-dihydroimidazo[2.1-*a*]phthalazin-6(5*H*)-one.
5. **6**: mp 234-236°C(from ethanol, as in Ref. 1); ms $M^{+\cdot}$ 229; ir(cm^{-1}) amide-I 1705, $\nu_{C=N}$ 1545 and 1595; ^{1}H-nmr CH_3CO 2.38 (s, 3H), -$(CH_2)_2$- 4.42 and 4.61 (A_2B_2, J = 9.4 Hz, 4H), ArH 7.8-8.4 (m, 4H).
   7: mp > 360°C (from ethanol), ms $M^{+\cdot}$ 274; ir(cm^{-1}) amide-I 1695, $\nu_{C=N}$ 1545 and 1595, ν_{NO_2} 1550 and 1375; ^{1}H-nmr CH_3CO 2.40 (s, 3H), -$(CH_2)_2$- 4.43 and 4.64 (A_2B_2, J = 9.4 Hz, 4H), ArH 7.9-8.3 (m, 3H).
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7. In **6** and **7** - as proved by DNOE measurements - the methyl group is in syn position to the aromatic ring, while in **8-11** the bulkier chloromethyl groups tend to occupy the anti position forcing the carbonyl oxygen to get into the proximity of the benzene ring.
8. The methylene shifts measured for the salts of **1** and **5** formed with chloroacetic acids vary between 4.1 and 4.5 ppm.
9. **12**: ^{13}C-Nmr C-1 83.0, C-2 163.2, C-4 59.3, C-5 47.4, C-6 168.4, C-6a 123.3, C-7,10a 146.5 and 146.8, C-8 127.5, C-9 136.8, C-10 129.6, C-10b 93.7, -$COCHCl_2$ 161.3 and 68.2.
10. **13**: mp 231-235°C (from ethyl acetate); ms $M^{+\cdot}$ 343; ir(cm^{-1})ν_{N-H} 3280, amide-I 1723 and 1743, ν_{NO_2} 1550 and 1350; ^{1}H-nmr -$(CH_2)_2$- 3.3-4.2 overlapping m's (4H), ArH 7.8-8.2 (m, 3H), N-H 11 30 (s, 1H); ^{13}C-nmr C-1 84.5, C-2 164.7, C-4 60.4, C-5 47.2, C-6 169.2, C-6a 124.4, C-7,10a 146.9 and 147.1, C-8 127.3, C-9 136.4, C-10 130.5, C-10b 96.6.
11. Ir spectra were registered in KBr pellets with a Zeiss Specord 75 Spectrophotometer Ms spectra were obtained with a KRATOS ms 50 double focused high resolution spectrometer (El. 70eV). ^{1}H and ^{13}C-nmr spectra were recorded in DMSO-d_6 (internal reference: DSS) at 80 MHz and 20 MHz, respectively, by a BRUKER AM-80 PFT instrument. Assignments of the carbon lines were proved by DEPT measurements.
12. Crystal data of compound **13**: $C_{12}H_8Cl_2N_4O_4$, M = 343.13, triclinic, space group $P\bar{1}$, a = 8.357(1)Å, b = 10.616(2)Å, c = 7.795(2)Å, α = 101.43(2)°, β = 97.60(2)°, γ = 89.75(2)°, V = 671.7(2)Å^3, Z = 2, D_{calc} = 1.696 g/cm^3, μ(CuKα radiation λ = 1.5418Å) = 46.09 cm^{-1}. Intensity data ($2\theta_{max}$ = 150.2°, 2666 non-equivalent reflections) were recorded on Rigaku AFC6S diffractometer (CuKα radiation, graphite monochromator). Crystal structure was solved by direct method. Full matrix least squares refinement of atomic parameters (anisotropic non-hydrogen atoms, only B's for hydrogens) converged at R = 0.069 (Rw = 0.064) over 1362 observations, respectively with $I > 3.0\sigma(I)$. Atomic parameters for **13** will be deposited at the Cambridge Crystallographic Data Centre.

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