Synthesis of new 1*H*-pyridazine derivatives *peri*-annelated with acenaphthene and acenaphthylene

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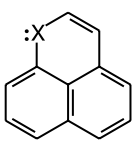
The reaction of 6-acetyl-5-hydroxyacenaphthene with methylhydrazine afforded 1,3-dimethyl-1*H*-6,7-dihydroacenaphtho[5,6-*de*]pyridazine. Its dehydrogenation with chloranil gave 1,3-dimethyl-1*H*-acenaphtho[5,6-*de*]pyridazine, which is a heteroaromatic compound with an essentially new topology of the π-system. The reaction of 3-methyl-1*H*-6,7-dihydroacenaphtho[5,6-*de*]pyridazine with 3,5-di-*tert*-butyl-1,2-benzoquinone yielded a dimer containing the acenaphthene and acenaphthylene moieties of *peri*-annelated 1*H*-1,2-diazines connected in positions 1´ and 9.

Key words: heteroaromatic systems, 14π-electron system, pyridazine, acenaphthene, acenaphthylene, "peridazine", "peridazylene".

The overwhelming majority of known heteroaromatic compounds and those under study represent 6π-electron five- or six-membered heterocycles or their *ortho*-annelated derivatives. A special case refers to *peri*-annelated naphthalene derivatives with a six- or seven-membered heterocycle[1] (*e.g.*, compounds **1** (X = O, S, and NR) and **2** (X = O^+, S^+, RN^+, and N)); although possessing $4n + 2$ π-electrons (n = 3), they cannot be treated as aromatic compounds because only 13 π-electrons are delocalized over the outer ("Hückel") contour, while the 14th one is at the central atom and is not involved in peripheral conjugation.



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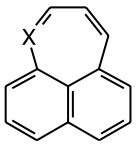

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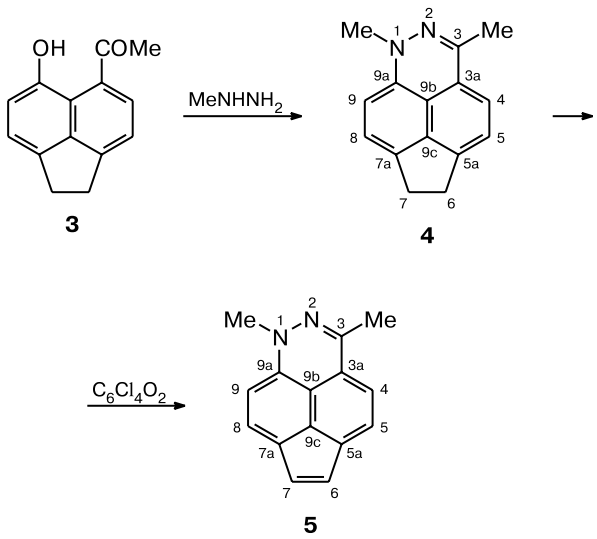
In the present work, by heating the earlier[2] described 6-acetyl-5-hydroxyacenaphthene **3** with methylhydrazine in ethanol, we obtained acenaphthopyridazine **4** (Scheme 1). Its dehydrogenation with *p*-chloranil gave a new heteroaromatic system, namely, 1,3-dimethyl-1*H*-indeno[6,7,1-*def*]cinnoline (**5**, IUPAC nomenclature), or—which is more customary in the nomenclature adopted for *peri*-annelated heterocycles—1,3-dimethyl-1*H*-acenaphtho[5,6-*de*]pyridazine. Hereafter, by analogy with heterocycles of the so-called perimidine series,[3,4] diazine **4** is named 1,3-dimethylaceperidazine and compound **5** is named 1,3-dimethylaceperidazylene.

Scheme 1



3 **4** **5**

It is correct to correlate acenaphthene and acenaphthylene diazines **4** and **5** with the isoelectronic hydrocarbons acepleiadiene **6** and acepleiadylene **7**.[5]* The seven-membered ring in acepleiadiene **6** is reported[5] to be of a distinct divinyl character, while acepleiadylene **7** is an aromatic compound.

The dominant role of the outer 14π-electron contour in compound **7** and a specific character of the endocyclic double bond occupying the non-bonding orbital were also

* The nomenclature of these hydrocarbons and some related notes were taken from O. E. Shelepin´s book.[6]

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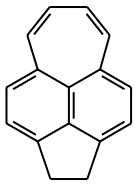

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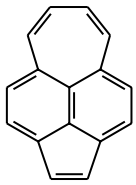

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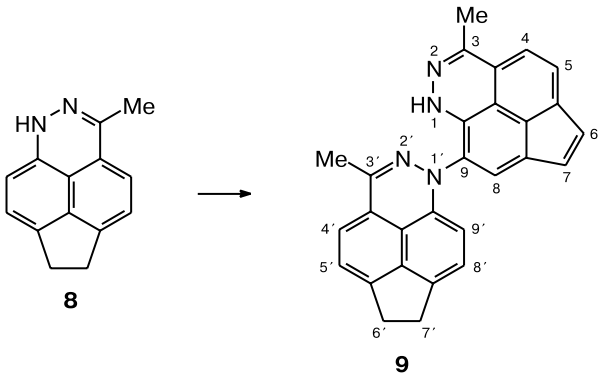
reported.[7,8] Such a comparison corrected for the difference between arenes and heteroaromatic analogs[9] seems to be valid for the *peri*-annelated diazines **4** and **5** synthesized by us. First representatives of heteroarenes with the π-system topology analogous to that in compounds **4** and **5** were obtained in the perimidine series.[3,4] Later studies[10] were devoted to some of their transformations illustrating the specific chemical behavior of these new heteroaromatic systems.

The differences between the ^{1}H NMR spectra of aceperidazine **4** and aceperidazylene **5** are of interest. For instance, signals for the aromatic protons in the spectrum of the former appear at δ 5.9 to 7.0, while for the latter, they are shifted downfield by 1.4 ppm (δ 7.1—8.5), which unambiguously indicates the aromatization of the heterocyclic system in the presence of a vinyl "bridge" in the *peri*-positions opposite to the heterocycle. The increase in the diamagnetic ring current as a manifestation of the aromaticity is also evident from the downfield shifts by 0.96 and 0.80 ppm of the signals for the protons of the methyl groups in positions 1 and 3, respectively, in the ^{1}H NMR spectra of 1,3-dimethylaceperidazylene **5** compared to 1,3-dimethylaceperidazine **4**. The protons of the vinylene bridge in aceperidazylene **5** resonate at δ 7.63 to 7.80; however, their spin-spin coupling constant (J = 4.1 Hz) is noticeably lower than that of the naphthalene protons (J = 7.5 and 8.1 Hz). The ^{1}H NMR spectrum of aceperidazine **4** shows characteristic signals for the naphthalene protons at C(5) and C(8) as doublets of triplets arising from spin-spin couplings of the aromatic protons at C(4) and C(9) with the bimethylene protons.

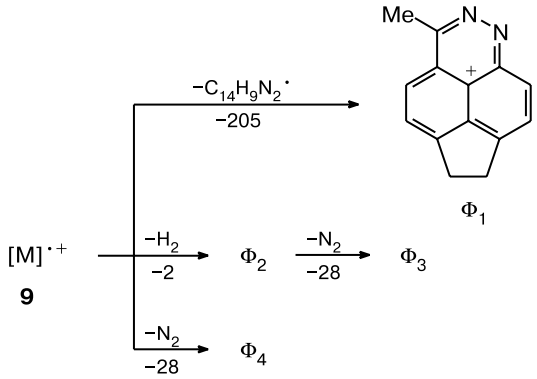
A different result was obtained in the reaction of 3-methylaceperidazine **8** (containing no alkyl substituent at the "pyrrole" heteroatom) with the oxidant 3,5-di-*tert*-butyl-1,2-benzoquinone (Scheme 2). An individual compound isolated from a complex mixture can be formulated as dimer **9** (^{1}H NMR, COSY, and MS data).

The dimeric structure of compound **9** was confirmed by the presence of the stable molecular ion $[M]^{\cdot+}$ (m/z = 412, I_{rel} = 100%) and the character of its fragmentation (Scheme 3). The most informative fragmentation pathways lead to cation Φ_1 (m/z = 207, I_{rel} = 50%), dehydrogenation product of the bimethylene fragment Φ_2 (m/z = 410, I_{rel} = 80%), and fragmentation ions Φ_3 (m/z = 382, I_{rel} = 60%) and Φ_4 (m/z = 384, I_{rel} = 70%) resulted from release of molecular nitrogen.

Scheme 2



Scheme 3



Because dimer **9** consists of the connected aceperidazine (pseudoaromatic) and aceperidazylene moieties (heteroaromatic), its ^{1}H NMR spectrum in the range of aromatic protons (δ 5.84—8.46) is essentially a superposition of the spectra of diazines **4** and **5**. The ^{1}H NMR spectrum of dimer **9** shows two signals for the protons of two magnetically nonequivalent methyl groups (s, 3 H); in addition, it contains two signals for the bimethylene fragment (br.t, 2 H), two signals for C(5′)H and C(8′)H (dt, 1 H), and two signals for C(4′)H and C(9′)H (d, 1 H), which are close to the signals observed for compound **4**, and four signals for C(4)H, C(5)H, C(6)H, and C(7)H (d, 1 H) with characteristic spin-spin coupling constants and a signal for C(8)H (s, 1 H), which are analogous to the corresponding signals for compound **5**; the low-field singlet at δ 10.7 for N(1)H suggests intramolecular hydrogen bonding. A comparison of the ^{1}H NMR spectra of dimer **9**, aceperidazine **4**, and aceperidazylene **5** allowed, with consideration of MS data and the electron densities calculated for the framework atoms of the heterocyclic system, unambiguous location of the connecting atoms in the moieties and assignment of the signal for each proton in the spectra of compounds **4**, **5**, and **9**.

The correctness of the signal assignment for dimer **9** was also confirmed by 2D (COSY) ^{1}H NMR spectrum

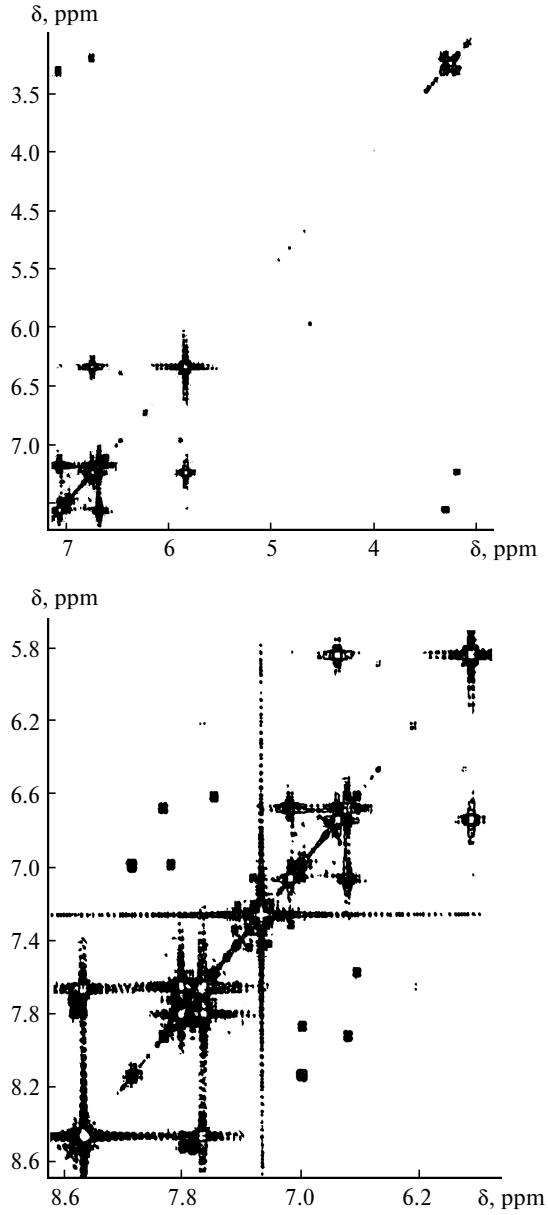


Fig. 1. 2D (COSY) ^{1}H NMR spectrum of dimer **9**.

showing distinct cross peaks due to spin-spin couplings between the protons (Fig. 1).

According to the quantum-chemical calculations (Fig. 2), diazines **4** and **5** belong to so-called π-abundant heterocycles[9] since all the framework atoms of the heterocyclic system (except for the "pyrrole" N atom in position 1) are negatively charged; this charge, in fact, is due to the electron-donating effect of the "pyrrole" heteroatom. It is worth noting that the negative charges at the vinylene atoms in aceperidazylene **5** (C(6), C(7)) are almost three times the charges at the atoms of the bimethylene group in aceperidazine **4**. These compounds should be expected to be highly reactive toward electro-

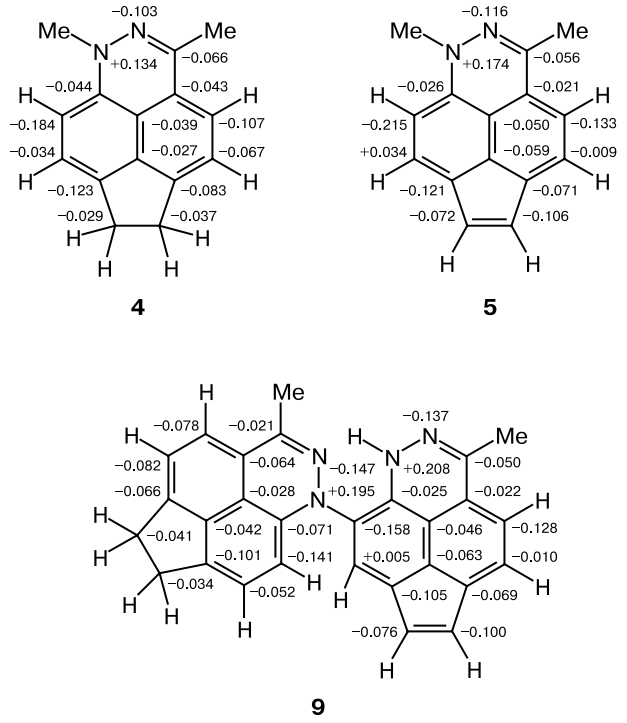


Fig. 2. PM3-calculated electron density distribution in compounds **4**, **5**, and **9**.

philic reagents, especially at positions 2, 4, 6, and 9, which bear the highest negative charges. An analogous order of the electron density distribution is retained in the acenaphthene and acenaphthylene fragments of dimer **9**.

Experimental

^{1}H NMR spectra were recorded on Bruker DPX-250 and Varian Unity-300 instruments (250 and 300 MHz, respectively) with $SiMe_4$ as the internal standard. IR spectra were recorded on a Specord IR75 spectrometer (Nujol). Mass spectra were recorded on a Finnigan MAT Incos 50 instrument (EI, 70 eV, direct inlet probe). Compounds were purified by column chromatography on alumina with chloroform as the eluent.

1,3-Dimethyl-1*H*-6,7-dihydroacenaphtho[5,6-*de*]pyridazine (4) (1,3-dimethylaceperidazine). A suspension of 5-acetyl-6-hydroxyacenaphthene (**3**) (0.5 g, 2.3 mmol) and methylhydrazine (0.15 mL, 2.8 mmol) in ethanol (3 mL) with two drops of acetic acid was refluxed for 7 h. The hot reaction mixture was filtered and the filtrate was evaporated to dryness. The residue was dissolved in chloroform and chromatographed on alumina. The solvent was removed to give compound **4** (0.46 g, 87%) as orange crystals, m.p. 128—129 °C. Found (%): C, 81.38; H, 6.04; N, 12.32. $C_{15}H_{14}N_2$. Calculated (%): C, 81.08; H, 6.31; N, 12.61. ^{1}H NMR ($CDCl_3$), δ: 2.07 (s, 3 H, C(3)H_3); 3.17 (t, 2 H, C(6)H_2, $J_{6,7}$ = 7.0 Hz); 3.27 (t, 2 H, C(7)H_2, $J_{7,6}$ = 7.0 Hz); 3.32 (s, 3 H, NMe); 5.92 (d, 1 H, H(9), $J_{9,8}$ = 7.5 Hz); 6.90 (d, 1 H, H(4), $J_{4,5}$ = 7.1 Hz); 6.95 (dt, 1 H, H(8), $J_{8,9}$ = 7.5 Hz, $J_{8,7}$ = 1.4 Hz); 6.98 (dt, 1 H, H(5), $J_{5,4}$ = 7.1 Hz, $J_{5,6}$ = 1.4 Hz).

1,3-Dimethyl-1*H*-acenaphtho[5,6-*de*]pyridazine (5) (1,3-dimethylaceperidazylene). A suspension of 1,3-dimethylaceperidazine (**4**) (0.35 g, 1.5 mmol) and *p*-chloranil (0.39 g, 1.5 mmol) in toluene was refluxed for 1 h. The hot reaction mixture was filtered and the filtrate was evaporated to dryness. The residue was dissolved in chloroform and chromatographed on alumina to give compound **5** (0.3 g, 86%) as golden yellow crystals, m.p. 158—160 °C. Found (%): C, 81.50; H, 5.23; N, 12.98. $C_{15}H_{12}N_2$. Calculated (%): C, 81.82; H, 5.45; N, 12.73. ^{1}H NMR ($CDCl_3$), δ: 2.87 (s, 3 H, C(3)H_3); 4.28 (s, 3 H, NMe); 7.15 (d, 1 H, H(9), $J_{9,8}$ = 8.1 Hz); 7.63 (d, 1 H, H(6), $J_{6,7}$ = 4.1 Hz); 7.78 (d, 1 H, H(4), $J_{4,5}$ = 7.5 Hz); 7.80 (d, 1 H, H(7), $J_{7,6}$ = 4.1 Hz); 8.37 (d, 1 H, H(8), $J_{8,9}$ = 8.1 Hz); 8.48 (d, 1 H, H(5), $J_{5,4}$ = 7.5 Hz).

3-Methyl-9-(3-methyl-1*H*-6,7-dihydroacenaphtho[5,6-*de*]pyridazin-1-yl)-1*H*-acenaphtho[5,6-*de*]pyridazine (9) (3-methyl-9-(3-methylaceperidazin-1-yl)aceperidazylene). A solution of 3,5-di-*tert*-butyl-1,2-benzoquinone (0.33 g, 1.5 mmol) in ether (3 mL) was added to a suspension of 3-methylaceperidazine (**8**)[11] (0.2 g, 1 mmol) in ether (10 mL). After three to five minutes, the reaction mixture became homogeneous. The solvent was removed and the resulting dark glassy substance was dissolved in chloroform and chromatographed on alumina to give compound **9** (0.1 g, 51%) as orange crystals, m.p. 145—147 °C. Found (%): C, 81.74; H, 4.71; N, 13.78. $C_{28}H_{20}N_4$. Calculated (%): C, 81.56; H, 4.85; N, 13.58. M = 412.28. MS, *m*/*z* (I_{rel} (%)): 413 $[M + 1]^{\bullet +}$ (35), 412 $[M]^{\bullet +}$ (100), 410 $[M - 2]^{\bullet +}$ (Φ_2, 80), 397 (40), 384 (Φ_4, 80), 382 (Φ_3, 60), 355 (20), 207 (Φ_1, 50), 57 (95), 41 (30). IR, ν/cm^{-1}: 2890 (NH), 1635, 1620, 1580 (C=N, arom.). ^{1}H NMR ($CDCl_3$), δ: 2.05 (s, 3 H, C(3′)H_3); 2.58 (s, 3 H, C(3)H_3); 3.20 (t, 2 H, C(6′)H_2, $J_{6',7'}$ = 7.0 Hz); 3.30 (t, 2 H, C(7′)H_2, $J_{7',6'}$ = 7.0 Hz); 5.84 (d, 1 H, C(9′)H, $J_{9',8'}$ = 7.6 Hz); 6.68 (d, 1 H, C(4′)H, $J_{4',5'}$ = 7.1 Hz); 6.74 (dt, 1 H, C(8′)H, $J_{8',9'}$ = 7.6 Hz, $J_{8',7'}$ = 1.4 Hz); 7.06 (dt, 1 H, C(5′)H, $J_{5',4'}$ = 7.1 Hz, $J_{5',6'}$ = 1.4 Hz); 7.65 (d, 1 H, H(6), $J_{6,7}$ = 4.6 Hz); 7.66 (d, 1 H, H(4), $J_{4,5}$ = 7.6 Hz); 7.80 (d, 1 H, H(7), $J_{7,6}$ = 4.6 Hz), 8.45 (s, 1 H, H(8)); 8.46 (d, 1 H, H(5), $J_{5,4}$ = 7.6 Hz); 10.70 (br.s, 1 H, (NH)).

References

1. V. V. Mezheritskii and V. V. Tkachenko, *Adv. Heterocycl. Chem.*, 1990, **51**, 1.
2. V. V. Mezheritskii, A. L. Pikus, and N. G. Tregub, *Zh. Org. Khim.*, 1991, **27**, 2198 [*J. Org. Chem. USSR*, 1991, **27** (Engl. Transl.)].
3. A. F. Pozharskii, T. I. Vinokurova, and V. G. Zaletov, *Khim. Geterotsikl. Soedin.*, 1976, 539 [*Chem. Heterocycl. Compd.*, 1976 (Engl. Transl.)].
4. T. I. Vinokurova and A. F. Pozharskii, *Khim. Geterotsikl. Soedin.*, 1976, 545 [*Chem. Heterocycl. Compd.*, 1976 (Engl. Transl.)].
5. V. Boekelheide and G. K. Vick, *J. Am. Chem. Soc.*, 1956, **78**, 653.
6. O. E. Shelepin, *Khimiya peritsiklicheskikh soedinenii* [*The Chemistry of Pericyclic Compounds*], Rostov. Gos. Univ., Rostov-on-Don, 1973, 240 (in Russian).
7. F. Gerson, E. Heilbronner, and V. Boekelheide, *Helv. Chim. Acta*, 1964, **47**, 1172.
8. P. D. Gardner and R. J. Thomson, *J. Org. Chem.*, 1957, **22**, 36.
9. A. F. Pozharskii, *Teoreticheskie osnovy khimii geterotsiklov* [*Theoretical Foundations of Heterocyclic Chemistry*], Khimiya, Moscow, 1985, 280 (in Russian).
10. I. S. Kashparov and A. F. Pozharskii, *Khim. Geterotsikl. Soedin.*, 1985, 372 [*Chem. Heterocycl. Compd.*, 1985 (Engl. Transl.)].
11. G. I. Bystritskii, G. N. Vorozhtsov, N. S. Dokunikhin, and S. V. Ovsyannikova, *Zh. Org. Khim.*, 1973, **9**, 1067 [*J. Org. Chem. USSR*, 1973, **9** (Engl. Transl.)].

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