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Structural Chemistry of Polycyclic Heteroaromatic Compounds. Part VII.† Photoelectron Spectra and Electronic Structures of Thienonaphthyridines. Part I

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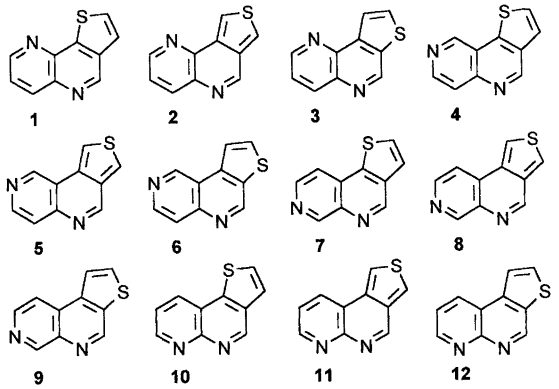
The He(I) photoelectron spectra of twelve isomeric thienonaphthyridines (**1–12**) are reported. Based on PM3 calculations, the ionization potentials (IP) have been assigned to molecular orbitals. The electronic structures are discussed according to first order perturbation theory. In particular, the effects of nitrogen lone pair interactions in the naphthyridine fragments on ionization potentials are investigated. Positional effects of the two nitrogen atoms are reflected in the energies of the π MOs and in the separation of the two n_N orbitals. The mode of annelation of the thiophene ring has a distinct effect on the energy of the first IP.

Naphthyridines are active as anti-inflammatory, antihypertensive, and immunosuppressive agents.[1] Thienonaphthyridine derivatives have proved useful as antitumor and antibacterial agents.[2] Apart from the biological activities, the annelation of π electron-rich with π electron-deficient aromatic compounds leads to interesting electronic and chemical properties. In a previous publication,[3] the electronic structures of thienoquinolines and thienoisoquinolines have been determined. The electronic structures were related to the parent π-isoelectronic hydrocarbon phenanthrene by first-order perturbation theory. This concept was useful in distinguishing isomers. The analysis of photoelectron (PE) spectra of a series of isomers instead of single compounds facilitates the safe assignment of ionization potentials to molecular orbitals. A similar study of heteroaromatic compounds with two nitrogen atoms was then of interest. In particular, the interactions of the two nitrogen lone pairs of thienonaphthyridines should be of interest. We have investigated 24 isomers in which the angular annelation of the thiophene and the two pyridine rings is the same as in the aforementioned thienoquinolines and thienoisoquinolines.[3] Because of the large number of isomers, we found it appropriate to report the results in two parts. In the first paper (Part I), the results for the isomers with the nitrogen atom of the central pyridine ring in position 5 are reported, while in the second paper (Part II) the isomers with this N atom in position 4 are dealt with.

Experimental

Materials. The syntheses of the isomeric thienonaphthyridines have been described in the literature: thieno[3,2-*c*][1,5]naphthyridine (**1**),[4] thieno[3,4-*c*][1,5]naphthyridine (**2**),[4] thieno[2,3-*c*][1,5]naphthyridine (**3**),[4] thieno[3,2-*c*][1,6]naphthyridine (**4**),[4] thieno[3,4-*c*][1,6]naphthyrid-



Scheme 1. Molecular formulae of thienonaphthyridines **1–12**.

† For Part VI see Ref. 3.
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ine (**5**),[4] thieno[2,3-*c*][1,6]naphthyridine (**6**),[4] thieno[3,2-*c*][1,7]naphthyridine (**7**),[5] thieno[3,4-*c*][1,7]naphthyridine (**8**),[5] thieno[2,3-*c*][1,7]naphthyridine (**9**),[5] thieno[3,2-*c*][1,8]naphthyridine (**10**),[5] thieno[3,4-*c*][1,8]naphthyridine (**11**)[5] and thieno[2,3-*c*][1,8]naphthyridine (**12**).[5]

Spectra and calculations. PE spectra were measured with a Leybold–Heraeus UPG 200 spectrometer equipped with an He(I) lamp (21.21 eV) as radiation source. The spectra were calibrated with the lines of xenon at 12.130 and 13.436 eV and of argon at 15.759 and 15.937 eV. The accuracy of the measurements was approximately ± 0.02 eV for ionization potentials; for broad or overlapping signals it was only about ± 0.05 eV. All compounds had to be heated to 70 °C to reach sufficient vapour pressure. The PM3 calculations[6] were performed with the MOPAC program.[7] All calculations were carried out with full geometry optimization.

Results and discussion

The PE spectra of compounds **1–12** are depicted in Figs. 1–4. IPs are summarized in Table 1, and the calculated orbital energies are given in Table 2.

The spectra were analysed with the aid of semiempirical PM3 calculations making use of Koopmans' theorem.[8] The MOs are classified according to their symmetry properties regarding the C_s symmetry of the molecules. There are seven doubly occupied π MOs, which are numbered with increasing energy, two n_N orbitals, which are termed n_I and n_{II}, and one n_S orbital. In addition, there are 21 occupied σ orbitals which give rise to broad and strongly overlapping ionization bands above 12 eV; only the first is given in Table 1. Also the ionizations correlated with π_1 and π_2 fall in this region and cannot be identified.

The first four π ionizations are located in the low energy region up to 11 eV. In most spectra, the first band

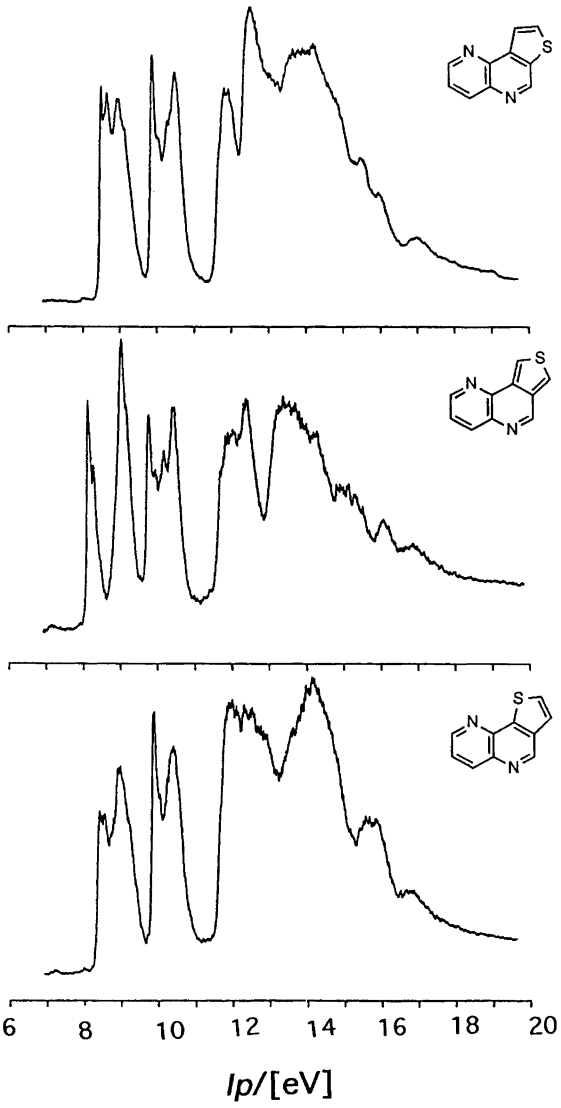

Fig. 1. PE spectra of thieno[1,5]naphthyridines **1–3**.

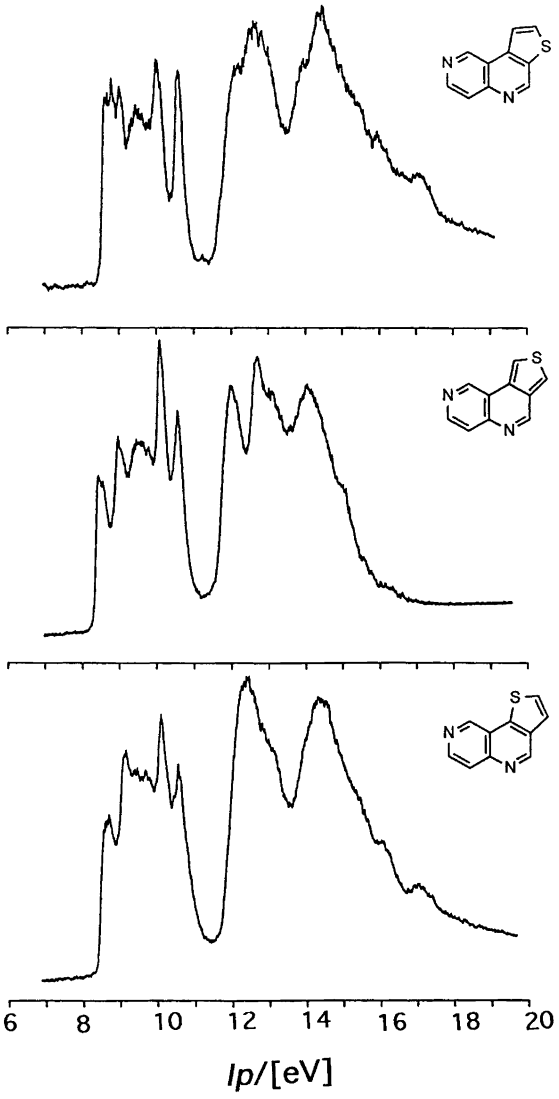

Fig. 2. PE spectra of thieno[1,6]naphthyridines **4–6**.

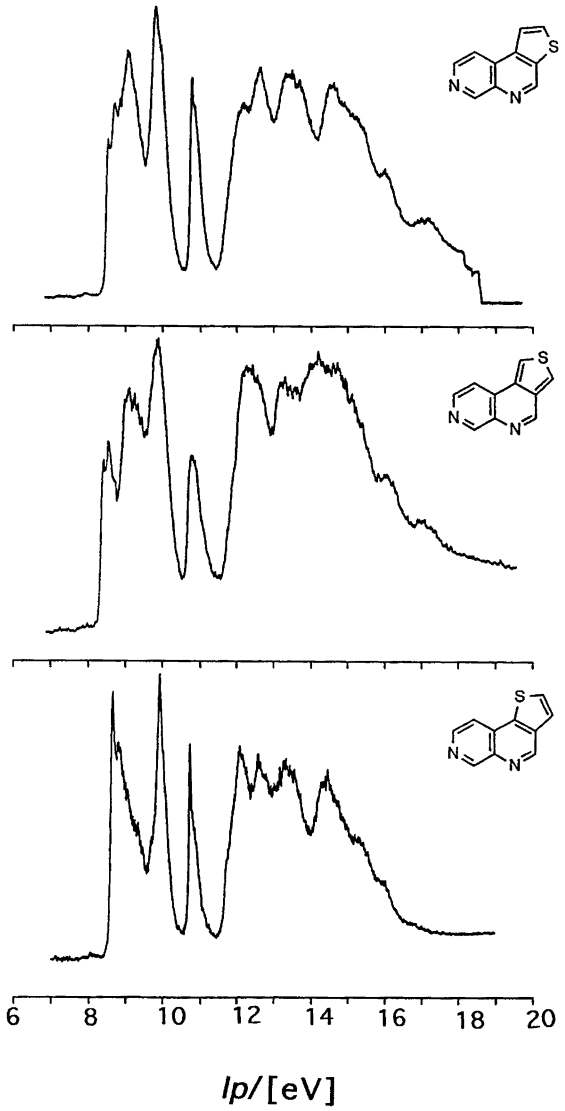

Fig. 3. PE spectra of thieno[1,7]naphthyridines **7–9**.

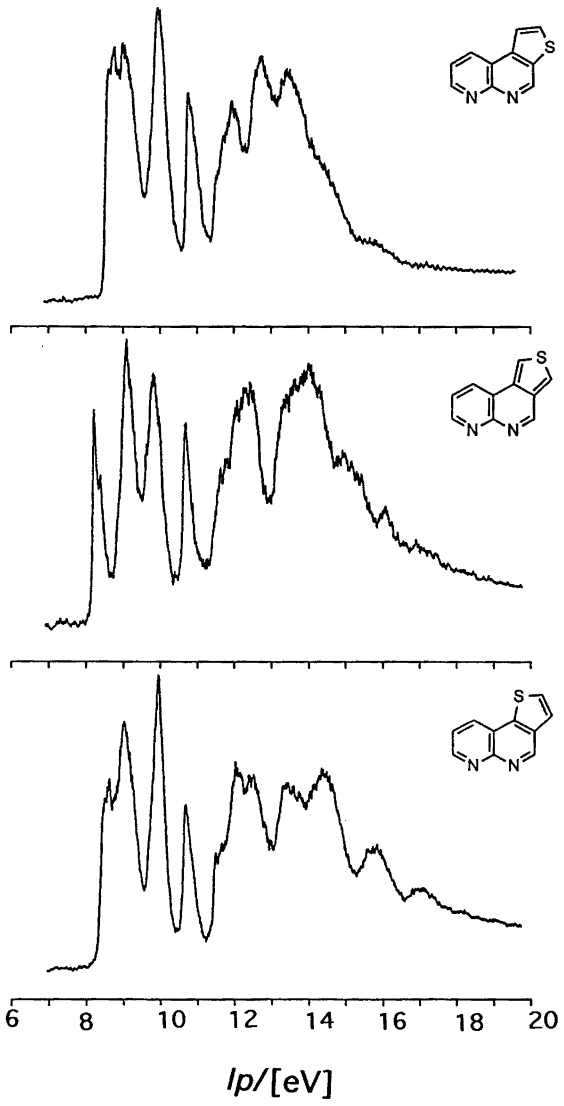

Fig. 4. PE spectra of thieno[1,8]naphthyridines **10–12**.

shows resolved vibrational fine structure indicating transitions to different vibrational states of the respective radical cations. The second band is well separated from the first one, except in the spectra of compounds **7** and **9** in which the first three bands are so close together that they form a single band. The shoulder in the high-energy region of this band is assigned to the n_{II} ionization. The

Table 1. Vertical ionization potentials IP_V (eV) and vibrational fine structure (cm^{-1}) of thienonaphthyridines **1–12**.

Compound	$\pi_7/7a''$	$\pi_6/6a''$	n_{II}/a'	$\pi_5/5a''$	n_I/a'	$\pi_4/4a''$	$\pi_3/3a''$	n_S/a'	σ/a'
1	8.42,1050	8.95	9.18	9.87,1300	10.24	10.43	11.96	12.13	12.33
2	8.13,1300	9.04	9.22	9.78,1400	10.20	10.44	11.93	12.38	12.40
3	8.48,1300	8.91	9.15	9.87,1200	10.28	10.48	11.90	12.04	12.54
4	8.65	9.11	9.50	10.10	9.75	10.56	12.42	12.25	12.55
5	8.42	8.97	9.38	10.09	9.66	10.55	12.63	12.10	12.70
6	8.61,1300	9.00	9.40	9.99	9.64	10.57	12.60	12.14	12.62
7	8.81	9.07	9.28	9.95	10.00	10.78	11.85	12.22	12.62
8	8.60	9.13	9.31	9.89	9.95	10.80	11.92	12.29	12.61
9	8.75	9.11	9.28	9.82	9.93	10.84	11.90	12.20	12.65
10	8.50,1400	9.05	9.27	9.96	10.04	10.70	11.61	12.11	12.48
11	8.26,1400	9.11	9.31	9.83	9.99	10.72	11.64	12.10	12.53
12	8.78	9.03	9.28	9.97	10.10	10.79	11.60	11.99	12.76

Table 2. Calculated enthalpies of formation ΔH_f (kJ mol^{-1}) and orbital energies $-\varepsilon^{PM3}$ (eV) of thienonaphthyridines **1–12**.

Compound	ΔH_f	π_7/7a″	π_6/6a″	n_{II}/a′	π_5/5a″	n_I/a′	π_4/4a″	π_3/3a″	n_S/a′	σ/a′
1	317.5	9.20	9.56	10.12	10.46	10.90	11.16	12.53	12.28	13.35
2	329.8	9.14	9.51	10.04	10.57	10.79	11.01	12.50	12.47	13.26
3	316.5	9.20	9.57	10.13	10.56	10.92	11.07	12.55	12.35	13.25
4	318.9	9.44	9.48	10.32	10.59	10.60	11.23	12.62	12.51	13.34
5	330.6	9.32	9.49	10.26	10.57	10.54	11.18	12.60	12.56	13.35
6	316.2	9.34	9.57	10.34	10.76	10.62	11.06	12.65	12.50	13.34
7	319.2	9.32	9.70	10.27	10.40	10.61	11.43	12.53	12.51	13.37
8	330.5	9.28	9.57	10.22	10.46	10.48	11.34	12.52	12.63	13.29
9	316.6	9.35	9.57	10.28	10.59	10.64	11.30	12.57	12.52	13.20
10	325.1	9.33	9.61	9.93	10.48	10.84	11.41	12.39	12.48	13.40
11	336.8	9.22	9.56	9.86	10.60	10.74	11.23	12.39	12.60	13.29
12	323.2	9.28	9.61	9.95	10.59	10.86	11.29	12.42	12.44	13.27

first three ionizations of compounds **4**, **5** and **6** lead to three different bands, but it is impossible to determine the vertical IP of the third band precisely. From comparison with the band intensities of n_N ionizations of azaphenanthrenes[9] it can be concluded that the third band results from two n_N ionizations. In the same way, the overlap of the fourth and fifth band in the spectra of compounds **7–12** is analysed and the ionizations are assigned to π_5 and n_I. In the spectra of compounds **1–3**, the n_I ionization appears as a shoulder on the low-energy side of the sixth band.

The accuracy of the assignments of calculated orbital energies ε_i to measured ionization potentials IP_i is confirmed by the linear regression $IP_i = 1.09(-\varepsilon_i) - 1.57$ with a correlation coefficient $r = 0.998$ (Fig. 5).

Energy differences $\Delta_i = (-\varepsilon_i) - IP_i$ up to 0.65 eV are found for the first IP. We observe large effects on this IP in compounds with the same naphthyridine fragment when the annelation of the thiophene ring varies. $IP(\pi_7)$ of compounds with a 3,4-annelated thiophene ring is lower than that of compounds with a 3,2- or 2,3-annelated thiophene ring. An explanation of this phenomenon is given by valence bond theory which is also useful for

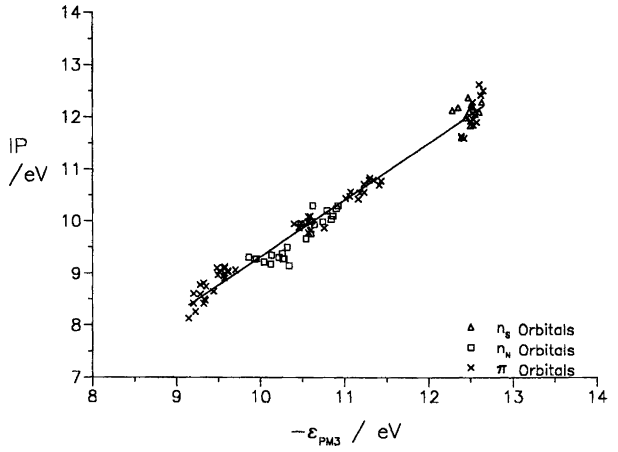

Fig. 5. Correlation diagram for ionization potentials IP_v and orbital energies $-\varepsilon^{PM3}$ of π, n_N and n_S orbitals of thienonaphthyridines **1–12**.

the estimation of the relative stabilities of isomers. Three Kekulé structures are possible for thienonaphthyridines with a 3,2- or 2,3-annelated thiophene ring, only two for compounds with a 3,4-annelated thiophene unit. The calculated enthalpies of formation (Table 2) of the 3,4-annelated thienonaphthyridines are approximately 13 kJ mol^{-1} larger than those of 3,2 and 2,3-annelated thienonaphthyridines. As has been observed previously, this difference in stability is often reflected in the energy of the HOMO.[10,11] This is a violation of the sulfur double bond model[12–14] which states that the substitution of a CC double bond by a sulfur atom is only a minor perturbation of the π electronic system.

Nearly the same values of $IP(\pi_7)$ are measured for compounds with a 3,2- or 2,3-annelated thiophene ring (**1** and **3**, **4** and **6**, **7** and **9**). An exception is observed for **10** and **12**, $IP(\pi_7)$ of **12** is 0.28 eV larger than that of **10**. According to first-order perturbation theory the electron distribution remains unchanged when CH is replaced by N and C = C is replaced by S. The change in energy is due to a change of the potential field in which the electrons move. This means that the shapes of the π MOs of thienonaphthyridines **1–12** are equivalent to those of the carbocyclic parent molecule phenanthrene.[3] We assume that only in **12** is an interaction of the electronegative nitrogen atom of the peripheral pyridine ring with the electropositive sulfur atom possible. In π_7 of phenanthrene[3] there is a bonding interaction between the atoms, where in **12** the nitrogen and the sulfur atoms are located. This interaction causes a stabilization of the HOMO of **12** relative to **10**. The π_7 ionization energy of phenanthrene[15] is 0.66 eV lower than the mean value measured for **1–12** (8.53 eV).

The π_6 ionization energies of **1–12** have a rather constant value close to 9.0 eV, independent of the mode of annelation. Also the calculated π_6 orbital energies vary in a rather narrow range.

Comparison with the spectra of naphthyridines[16] suggests that the n_N ionizations of **1–12** form broad bands of low intensity due to the bonding character of the corresponding MOs. The interaction of the two electron lone pairs results in two different IPs, which are located close to π ionizations. Fortunately, the investigation of several

isomers facilitates the correct identification and the positions of bands can be determined even in cases of strong overlap.

As can be seen in the correlation diagram in Fig. 6, ionizations originating from π_4 and π_3 are little affected by different annelation of the thiophene ring. The π_5 ionization, in which **7–12** is overlapped by the n_I ionization, is found between 9.8 and 10.1 eV. The corresponding ionization band of **1–6** is extraordinarily sharp, so that this MO must be largely non-bonding. Compounds **4–6** are characterized by high IP(π_5) values (10.0–10.1 eV). Only the nitrogen atom in the peripheral pyridine ring is responsible for this effect, because the nitrogen atom in the central ring is in the same position in all isomers. By first-order perturbation theory we can expect a stabilization of these MOs because in the positions of the nitrogen atoms there are large coefficients in π_5 of phenanthrene.[3]

Marked and characteristic effects are also observed for π_4. Isomers **1–6**, in which the nitrogen atom is in the upper half of the peripheral pyridine ring, show a destabilization of π_4 relative to isomers **7–12**, in which the nitrogen atom is in the lower half. For **1–6** we find small coefficients in the respective positions of phenanthrene.[3] In accord with the high IP(π_5) values of **7–12**, large coefficients are found in phenanthrene[3] in the positions of the nitrogen atom.

The π_3 ionizations are found above 11.5 eV. A noteworthy low value is observed for thieno[1,8]naphthyridines **10–12**; π_3 of phenanthrene[3] also has very small coefficients in the positions corresponding to the N atoms in the peripheral pyridine ring of **10–12**. The spectra of **1–3** and **7–9** reveal a higher and relatively constant IP(π_3) (11.91 ± 0.06 eV). Large and nearly equal coefficients in the corresponding positions of the N atoms of phenanthrene[3] are perceptible. In **4–6** the ionizations originating from π_3 lead to very high IP values (12.42–12.63 eV). This is in accord with large coefficients of π_3 in the N positions. The level ordering for π_3 (**10–12** > **1–3**, **7–9** > **4–6**) is in agreement with the PM3 results, although the calculated stabilization of π_3 of **4–6** relative to the other isomers is somewhat smaller than measured.

The n_S ionizations fall in a rather narrow range (12.16 ± 0.22 eV) and obviously do not permit any conclusion to be drawn regarding the annelation mode of the thiophene ring.

The energy split Δn_N of the two n_N ionizations (n_I and n_{II}) and its structural variation is of special interest and will be analysed in more detail. The corresponding IPs of thieno-1,5-naphthyridines **1–3** differ in energy by about 1.1 eV, those of thieno[1,6]naphthyridines **4–6** by about 0.3 eV, those of thieno[1,7]naphthyridines **7–9** by about 0.7 eV, and those of thieno[1,8]naphthyridines **10–12** by about 0.8 eV. These Δn_N values are in good agreement with the corresponding values observed for naphthyridines[16] and are nearly independent of the annelation of the thiophene ring.

The relative size of the observed Δn_N values can be estimated by qualitative MO theory. The interaction of the lone pairs n_1 and n_2 of the two nitrogen atoms can be separated into a through-bond and a through-space interaction.[17] The largest interaction is to be expected in **1–3** and **10–12**. In these molecules n_1 and n_2 have nearly equal coefficients in both n_N orbitals because of the twofold symmetry of the naphthyridine fragments (point groups C_{2v} or C_{2h}), and there should be effective through-bond interaction between the two n_N orbitals via σ orbitals because both n_1 and n_2 overlap with the same σ bonds. As is shown in Fig. 7 for compounds **10–12**, the two types of interaction partially compensate each other. Through-space interaction places n_I above n_{II}, but the level ordering is reversed by through-bond interaction. The nitrogen lone pairs n_1 and n_2 interact with occupied σ orbitals of the same symmetry as their linear combinations $n_1 + n_2$ and $n_1 - n_2$. In Fig. 7 only the p orbital with the dominant interaction is depicted. By the through-space interaction in **10–12** the split of n_I and n_{II} is reduced relative to **1–3**. This prediction of level ordering is supported by the description of the dehydronaphthalene diradical by Hoffmann[13] and is in accord with the PM3 calculations.

In the case of **4–6** and **7–9**, the two nitrogen atoms are estimated to be 420 pm and 370 pm, respectively, apart from each other, so that through-space interaction can be

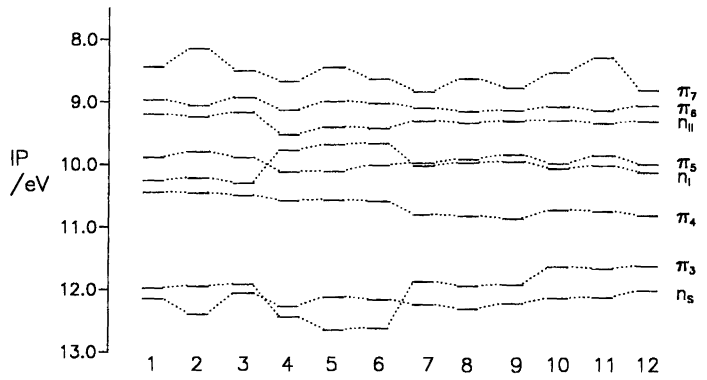

Fig. 6. Correlation diagram for ionization potentials of thienonaphthyridines **1–12**.

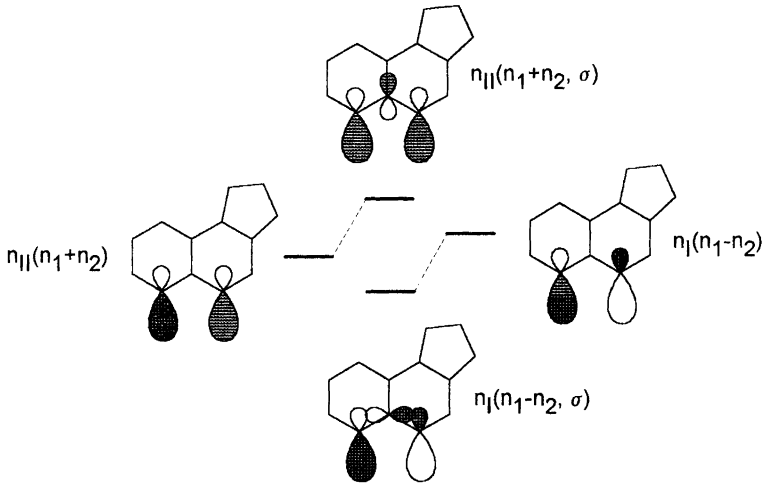

Fig. 7. Energy split of the nitrogen lone pairs orbitals n_I and n_{II} by through-space and through-bond interactions of n_1 and n_2.

neglected. Through-bond interaction can also be expected to be small because n_1 and n_2 experience poor overlap with the same σ bonds. In **4–6**, where the two nitrogen atoms are separated by four bonds, the n_N orbitals are nearly degenerate.

Some general conclusions which can be obtained from the investigation of isomeric thienonaphthyridines will be outlined in Part II.

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