N,N′-Bridged 1,4,5,8-Tetrakis(methylamino)naphthalenes and Their Radical Cations. Comparison with 1,4,5,8-Tetrakis(dimethylamino)naphthalene and Related Radical Cations†

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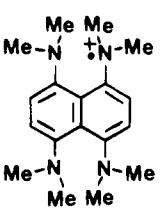
Received December 22, 1994®

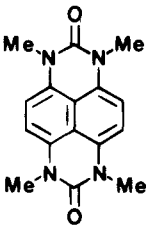
Syntheses of 3,8-dihydro-1,3,6,8-tetramethylpyrimido[4,5,6-*gh*]perimidine-2,7-(1*H*,6*H*)-dione (**2**), 1,2,3,6,7,8-hexahydro-1,3,6,8-tetramethylpyrimido[4,5,6-*gh*]perimidine (**3**), and 3,6,7,8-tetrahydro-1,3,6,8-tetramethylpyrimido[4,5,6-*gh*]perimidin-2(1*H*)-one (**4**) are reported. The corresponding radical cations were generated by oxidation with iodine or tris(4-bromophenyl)amminium hexachloroantimonate and were studied by ESR and ENDOR for comparison with the 1,4,5,8-tetrakis(dimethylamino)naphthalene radical cation ($\mathbf{1}^{\bullet+}$). The ESR results of $\mathbf{2}^{\bullet+}$–$\mathbf{4}^{\bullet+}$, however, give no indications which could explain the widely different *exo* (3.54 G) and *endo* (1.77 G) *N*-methyl proton splittings in $\mathbf{1}^{\bullet+}$.

The unusual properties of the strong electron-donor and "double proton sponge" 1,4,5,8-tetrakis(dimethylamino)naphthalene (**1**),[1,2] combining formally two 1,4-bis(dimethylamino)benzene units with two *peri*-arrangements of dimethylamino groups, are of special interest. The ESR spectrum of the radical cation $\mathbf{1}^{\bullet+}$, generated by oxidation of **1** with iodine or by electron transfer with tris(4-bromophenyl)amminium hexachloroantimonate, reveals significantly different *N*-methyl proton hyperfine coupling constants [a(H,NCH$_3$): 3.54 (12H) and 1.77 G (12H)].[1] A restricted rotation about the C_{aryl}–N bond would lead to different environments of the *N*-methyl groups corresponding to *endo* and *exo* arrangements of CH_3 in the NMe_2 substitutents. The striking feature of these splittings is their extraordinary difference in magnitude, almost 2:1. ESR studies of selectively *cis*- or *trans*-methyl-substituted allyl radicals[3,4] and 1,2-bis(dialkylamino)benzene radical cations[5] have shown unambiguously that the *exo*(*trans*) methyl proton splitting is larger than the *endo*(*cis*) one, e.g., 16.4 versus 14.0 G[3,4] or 7.19 versus 6.78 G.[5] With these species, however, the ratio of the *exo* and *endo* splittings is considerably smaller. The 2:1 ratio of $\mathbf{1}^{\bullet+}$ can hardly be explained by a conventional environmental effect only.

The close proximity of the *endo N*-methyl groups in $\mathbf{1}^{\bullet+}$ should cause strong steric hindrance preventing full planarity of the radical cation. Therefore, the unusual 2:1 ratio of the *exo*/*endo* a(H, NCH$_3$) splittings might have its origin in a special molecular arrangement of $\mathbf{1}^{\bullet+}$ leading to specific intramolecular interactions. From that point of view related cyclic compounds, e.g., **2**–**4**, are of interest. Owing to their cyclic structures, these compounds are better defined in their spatial arrangement and undergo less molecular reorganization on oxidation to the corresponding radical cations. For $\mathbf{1}^{\bullet+}$ and $\mathbf{3}^{\bullet+}$ qualitative McLachlan calculations indicate a SOMO which is antisymmetric about the C(4a)···C(8a) ($\mathbf{1}^{\bullet+}$) or C(2)···C(7) axis ($\mathbf{3}^{\bullet+}$). Accordingly, the SOMO coefficients at the adjacent nitrogens are equal but of opposite sign, and the bridging methylene groups of $\mathbf{3}^{\bullet+}$ reside in the nodal plane of the SOMO. For a methylene group interacting with two spin sites, Whiffen[6,7] has proposed within the framework of simple HMO theory that the proton hyperfine coupling constant is proportional to the square of the sum of the SOMO coefficients rather than to the sum of the corresponding squared terms. Therefore, in the case of $\mathbf{3}^{\bullet+}$ only a very small proton splitting is expected. In this paper we report on the syntheses of **2**–**4** and the characterization of their radical cations. The findings are compared with the properties of $\mathbf{1}^{\bullet+}$ and those of related radical cations.



$\mathbf{1}^{\bullet+}$



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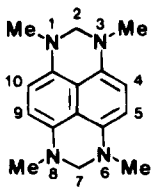

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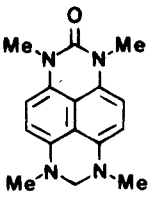

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† Dedicated to Professor Glen A. Russell on the occasion of his 70th birthday.

® Abstract published in *Advance ACS Abstracts*, July 1, 1995.

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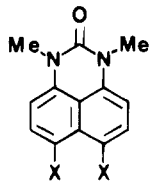
The synthesis of 3,8-dihydro-1,3,6,8-tetramethylpyrimido[4,5,6-*gh*]perimidine-2,7(1*H*,6*H*)-dione (**2**) has been accomplished starting from 1,3-dimethyl-6,7-dinitro-1*H*-perimidin-2(3*H*)-one (**5**).[1] Catalytic hydrogenation (5% Pd on charcoal) in dimethylformamide afforded the 6,7-diamino compound **6** which, owing to its laborious purification, was directly converted by a double reaction with diethyl dicarbonate into the corresponding 6,7-bis(ethyl carbamate) **7** (overall yield 66%). Subsequent methylation with methyl iodide in the presence of barium oxide provided the 6,7-bis[(ethoxycarbonyl)methylamino] derivative **8** as colorless needles from ethanol/pentane (47%). In the mass spectrum of **8**, the appearance of the *m/z* 296 fragment ion ($M^{\bullet+} - CO_2CH_2CH_3 - OCH_2CH_3$; 31% abundance) pointed to the possibility of a thermal ring closure of **8**. Indeed, pyrolysis of **8** at 700 °C in vacuo (0.001 mbar) led to the formation of **2** in low yield (14%). In accordance with its symmetric structure the ^{1}H NMR spectrum of **2** shows only singlets, namely the signal of the *N*-methyl hydrogens at $\delta = 3.22$ and that of the ring hydrogens at $\delta = 6.57$.



5: X = NO_2
6: X = NH_2
7: X = NHCOOEt
8: X = NMeCOOEt

Reduction of **2** with excess of lithium aluminium hydride in tetrahydrofuran afforded directly the target compound 1,2,3,6,7,8-hexahydro-1,3,6,8-tetramethylpyrimido[4,5,6-*gh*]perimidine (**3**) as yellow needles from ethanol (36%). For steric reasons **3** exists probably as flat boat and chair conformers possessing diastereotopic methylene hydrogens. The ^{1}H NMR spectrum of **3**, showing three singlets at $\delta = 2.81$ (12H, CH_3), 3.91 (4H, CH_2), and 6.47 (4-, 5-, 9-, 10-H), remains unchanged down to 215 K. In particular, no broadening of the methylene proton singlet was observed, indicating that the ring inversions of **3** in the studied temperature range are rapid on the NMR time scale. Measurements at lower temperatures were not possible owing to the low solubility. Similar reduction of **2** with lithium aluminum deuteride yielded **3D**, in which the methylene bridges are thoroughly deuterated as indicated by the disappearance of the proton signal at $\delta = 3.91$.

Introduction of methyl groups into primary amines by reductive alkylation with formaldehyde has proved to be a very useful method. Hence, starting from **6** and using this method, there was a possibility that in addition to *N*-methylation a simultaneous ring closure with formaldehyde could lead to the formation of 3,6,7,8-tetrahydro-1,3,6,8-tetramethylpyrimido[4,5,6-*gh*]perimidin-2(1*H*)-one (**4**). Therefore, compound **6** was treated with 37% aqueous formaldehyde solution in the presence of sodium cyanoborohydride according to the method of Borch and Hassid.[8] Careful workup of the reaction mixture provided **4** in very low yield (2%) as yellow needles from toluene. The ^{1}H NMR spectrum of **4** showed, as expected, two doublets at $\delta = 6.58$ ($J = 8.0$ Hz, 4-, 10-H) and 6.52 (5-, 9-H) and three singlets at $\delta = 3.99$ (2H, CH_2), 3.26 (6H, 1-, 3-NCH_3), and 2.85 (6H, 6-, 8-NCH_3). Assignments are based on NOE and on the chemical shifts of the NCH_3 protons in comparison to the ^{1}H NMR data of **2** and **3**. The mass spectrum [e.g., *m/z* 282 ($M^{\bullet+}$, 100%] and IR absorptions [e.g., $\nu = 1640$ cm^{-1} (CO)] also support structure **4**.

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Table 1. Oxidation Potentials and Peak Separations of 1, 2, 3 and 4 in Acetonitrile/0.1 M Tetrabutylammonium Perchlorate[a]

	E_1^0 (±0.01)/V	E_2^0 (±0.01)/V	$\Delta E_p = E_{pa} - E_{pc}$ /mV
1	−0.50[b]		40
2	+0.01	+0.43	72; 65
3	−0.42	−0.26	65; 65
4	−0.22	+0.12	68; 65

[a] Glassy carbon electrode versus Ag/AgCl; reference ferrocene ($E_1^0 = 0.352$ V) set to 0.00 V. [b] $E_{1,2}^0$.

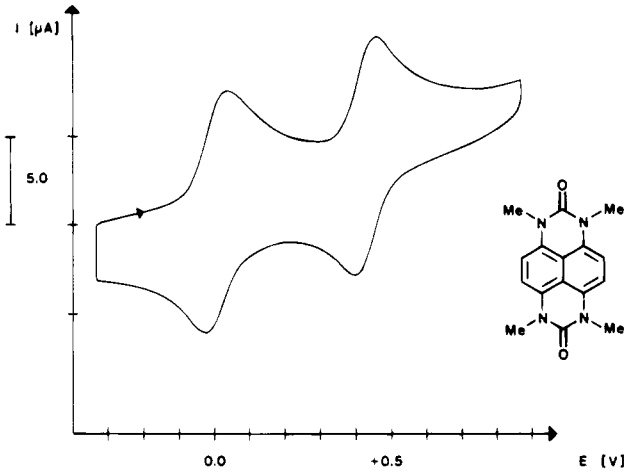

Figure 1. Cyclic voltammogram of **2** in acetonitrile/0.1 M tetrabutylammonium perchlorate, $\upsilon = 100$ mV s^{-1}.

Cyclovoltammetry proves that compound **3** is a very strong electron donor. The oxidation potentials of **2**–**4** in acetonitrile/0.1 M tetrabutylammonium perchlorate measured with a "glassy carbon electrode" versus Ag/AgCl are given in Table 1. All data are referred to ferrocene (Fc); Fc/Fc^+ was set to 0.00 V. In contrast to **1**, which demonstrated a reversible "two-electron" transfer composed of two superimposed one-electron steps, the cyclovoltammograms of **2**–**4** show two clearly separated and reversible one-electron oxidation steps. Figure 1 presents the cyclovoltammogram of **2** which is also characteristic for those of **3** and **4**. Further oxidation of the dications $\mathbf{2}^{2+}$, $\mathbf{3}^{2-}$, and $\mathbf{4}^{2+}$ to the corresponding trications was found to be irreversible. Therefore, *E* potentials could not be determined.

Surprisingly, the first oxidation potential of the almost planar **3** ($E = -0.42$ V) is higher than that of the "two-electron" transfer of **1** ($E = -0.50$ V). This unusual result is apparently caused by the fact that the considerable steric strain of **1**, induced by the dimethylamino groups in the *peri*-positions and leading to a clear deviation of the naphthalene skeleton from planarity, is partly released in the formation of the radical cation $\mathbf{1}^{\bullet+}$.[1,2] Successive replacement of the methylene bridges in **3** by the electron attracting carbonyl function enhances, as expected, the oxidation potentials (Table 1) and increases the difference between the first and second oxidation potential: $E - E = 0.16$ (**3**), 0.34 (**4**), 0.42 V(**2**).

Owing to the very low oxidation potential of **3** the corresponding radical cation $\mathbf{3}^{\bullet+}$ is readily formed by oxidation with iodine. Less persistent are the radical cations $\mathbf{2}^{\bullet+}$ and $\mathbf{4}^{\bullet+}$ which were generated in toluene–

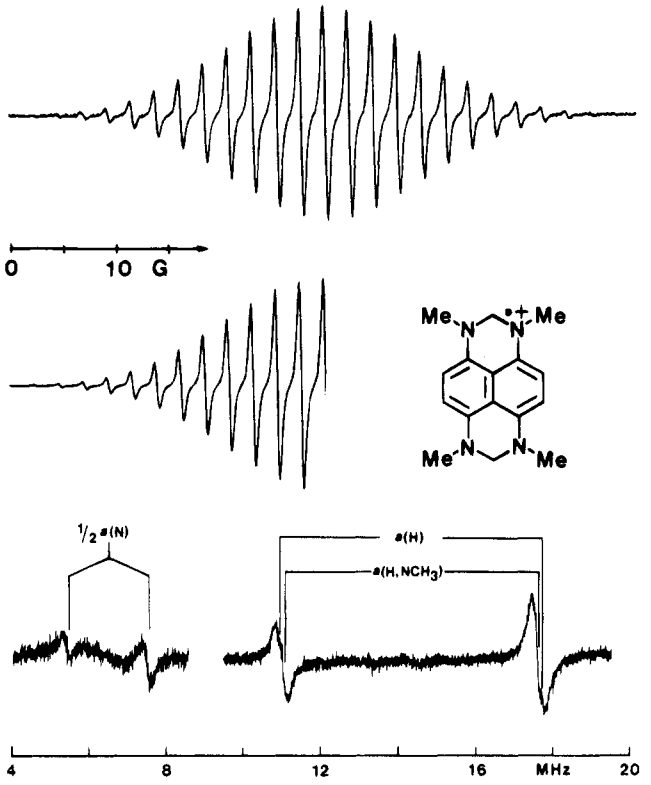

Figure 2. Radical cation $3^{\bullet+}$ in dichloromethane at 220 K: ESR spectrum together with a simulation using the data in Table 2 (top) and ENDOR spectrum (bottom).

trifluoroacetic acid (19:1) at 260 K using tris(4-bromophenyl)amminium hexachloroantimonate ($4^{\bullet+}$) or 3-chloroperoxybenzoic acid ($2^{\bullet+}$) as oxidant.

The ESR spectra of $2^{\bullet+}$ and $3^{\bullet+}$ (Figure 2) are only partially resolved showing simple sets of superimposed lines. Better resolved is the complex ESR spectrum of $4^{\bullet+}$ (Figure 3) which could also not be directly analyzed. ENDOR studies of these radical cations provide more information. The ENDOR spectra of $2^{\bullet+}$ at 260 K and of $3^{\bullet+}$ at 220 K (Figure 2) clearly show the ^{14}N line pair. In addition, only one broad ^1H line pair is observed which, however, consists of two superimposed ^1H line pairs as indicated by weak shoulders (Figure 2). General triple experiments[9] confirm the presence of two close ^1H line pairs and reveal, moreover, that these splittings have opposite signs. The missing third ^1H line pair of $3^{\bullet+}$ is clearly detected only at 260 K. Attempts to determine its relative sign failed due to the fact that the other two ^1H line pairs do not resolve at this temperature. Multiplicities of the different sets of equivalent hydrogens and consequently their assignment were derived from the corresponding ESR spectra which are well simulated using the data given in Table 2. As predicted by the Whiffen rule,[6,7] the methylene proton splitting of $3^{\bullet+}$ is extremely small, 0.14 G at 260 K, and deuteration of these protons ($3D^{\bullet+}$) leaves the ESR spectrum almost unaffected.

In nitrogen-centered radical cations with $RN^{\bullet+}Me_2$ structures the $a(H, NCH_3)/a(N)$ ratio depends sensitively on the equilibrium geometry at the nitrogen center.[10] Ratios ≥ 1 point to a planar $N^{\bullet+}$ geometry. Typical

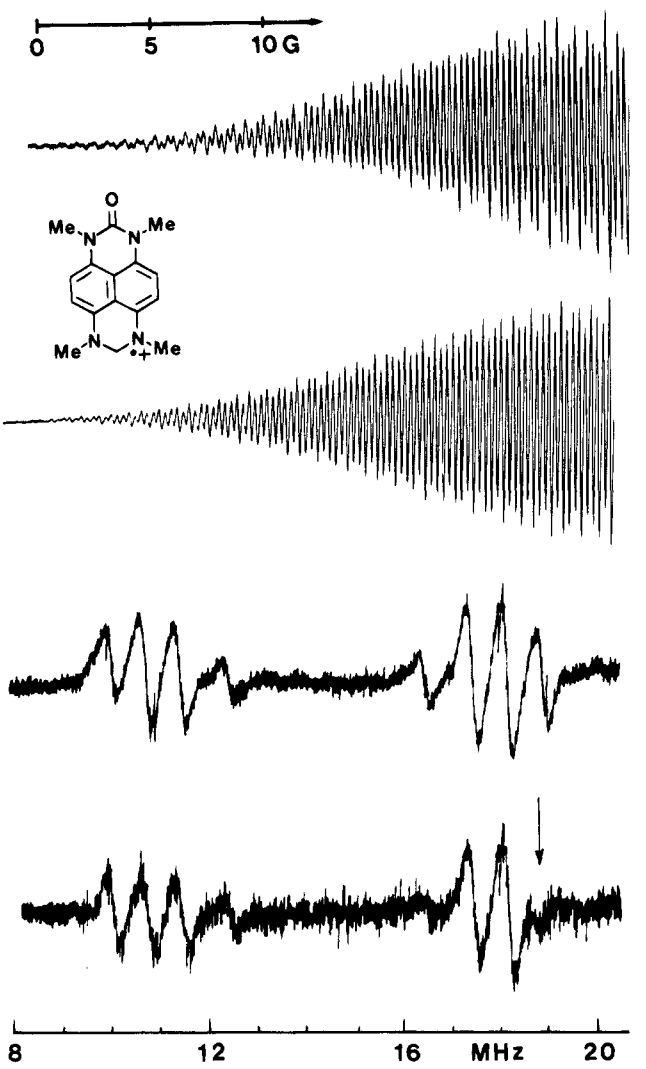

Figure 3. Radical cation $4^{\bullet+}$ in toluene–trifluoroacetic acid (19:1) at 260 K: Low field half of the ESR spectrum together with a simulation using the data in Table 2 (top) and ^1H ENDOR spectrum together with a general triple resonance spectrum, pump frequency 19.92 MHz (bottom).

examples are $N^{\bullet+}Me_3$, 1.39,[11] and $PhN^{\bullet+}Me_2$, 1.09.[12] When the planar equilibrium geometry is destabilized, e.g., by steric or conformational effects, the spin-bearing orbital at the nitrogen gains some s-character leading to a significant increase of $a(N)$ and, hence, to a clear decrease of the $a(H, NCH_3)/a(N)$ ratio. The $a(H, NCH_3)/a(N) = 0.95$ ratio of $2^{\bullet+}$ agrees well with a planar structure. In the case of $3^{\bullet+}$, however, the small $a(H, NCH_3)/a(N) = 0.51$ ratio and, in addition, the pronounced negative temperature coefficient of $a(N)$ (300 K: 4.37, 260 K: 4.47, 220 K: 4.60 G) indicate that the equilibrium geometry at the nitrogens deviates slightly from planarity. Since no steric effects are involved, the results can be taken as evidence that $3^{\bullet+}$ probably exists as very flat boat and chair conformers which at 260 K invert rapidly with respect to the ESR time scale.

As expected, the ENDOR spectrum of $4^{\bullet+}$ revealed four ^1H coupling constants and general triple resonance experiments[9] provided their relative signs (Figure 3). On

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Table 2. Isotropic Hyperfine Coupling Constants and *g*-Values of the Radical Cations $1^{\bullet+}$, $2^{\bullet+}$, $3^{\bullet+}$, $4^{\bullet+}$, $9^{\bullet+}$, and $10^{\bullet+}$

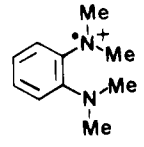
	method	T/K	a(N)/G	a(H, NCH_3)/G	a(H)/G	a(H, CH_2)/G	a(H, NCH_3)/a(N)	g	ref
$1^{\bullet+}$	ESR[a]	220	2.65 (4N)	3.54 (12H), 1.77 (12H)	1.53 (4H)		1.34, 0.67	2.0029	1
	ENDOR[a]	220		+3.55, +1.78	−1.51				
$2^{\bullet+}$	ESR[b]	260	2.44 (4N)	2.34 (12H)	2.41 (4H)			2.0028	
	ENDOR	260	2.46	+2.34	−2.41		0.95		
$3^{\bullet+}$	ESR[a]	220	4.58 (4N)	2.33 (12H)	2.46 (4H)			2.0028	
	ENDOR[a]	220	4.60	+2.33	−2.42		0.51		
	ESR[a]	260	4.47 (4N)	2.37 (12H)	2.37 (4H)				
	ENDOR[a]	260	4.47	2.33	2.33	0.14			
	ESR[a]	300	4.37 (4N)	2.36 (12H)	2.36 (4H)			2.0028	
$3D^{\bullet+}$	ESR[a]	300	4.37 (4N)	2.36 (12H)	2.36 (4H)				
$4^{\bullet+}$	ESR[b]	260	5.59 (6,8-N), 2.12 (1,3-N)	2.64 (6H),[c] 2.10 (6H)[d]	3.21 (2H),[e] 1.34 (2H)[e]		0.47, 0.99	2.0028	
	ENDOR[b]	260		+2.63, +2.13	−3.14, −1.43				
$9^{\bullet+}$	ESR[a]	200	6.95 (2N)	7.19 (6H), 6.78 (6H)	2.22 (4,5-H)		1.03, 0.98	2.0031	5
$10^{\bullet+}$	ESR[f]	220	3.65 (4N)	(+)3.76 (12H), (+)2.56 (12H)	(+)0.34 (3,6-H)		1.03, 0.70	2.0031	13

[a] In dichloromethane. [b] In toluene–trifluoroacetic acid (19:1). [c] a(H, 6,8-NCH_3). [d] a(H, 1,3-NCH_3). [e] No specific assignment. [f] In ethanol–dichloromethane (4:1).

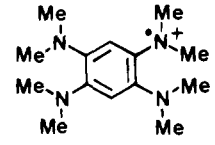
the basis of these results, the complex ESR spectrum of $4^{\bullet+}$ was well simulated using the data given in Table 2. It is assumed that the a(H, NCH_3)/a(N) ratios of $2^{\bullet+}$ and $3^{\bullet+}$ are also valid for the partial structures of $4^{\bullet+}$; therefore, the tentative assignment of the a(N) and a(H, NCH_3) coupling constants can be made as in Table 2. The assignment of the ring proton coupling constants, on the other hand, remains open.

As confirmed by the ESR results, the SOMO's of $1^{\bullet+}$ and $3^{\bullet+}$ are antisymmetric about the C(4a)···C(8a) and C(2)···C(7) axis, respectively, and the coefficients at the adjacent nitrogens are equal in magnitude and have opposite signs. This could lead to the conclusion that in $1^{\bullet+}$ the arrangement of the *endo* *N*-methyl groups close to the nodal plane in the C(4a)···C(8a) axis might affect and, hence, reduce the *endo* NCH_3 proton splitting.

ESR results of related radical cations, however, e.g., 1,2-bis(dimethylamino)- ($9^{\bullet+}$)[5] and 1,2,4,5-tetrakis(dimethylamino)benzene radical cation ($10^{\bullet+}$),[13] do not agree with this view. Contrary to $1^{\bullet+}$ in both $9^{\bullet+}$ and $10^{\bullet+}$ the SOMO coefficients at the adjacent nitrogens have the same sign. ESR studies of $9^{\bullet+}$ have led to an unambiguous assignment of the *exo* and *endo* methyl proton splittings (*exo*: 7.19 G; *endo*: 6.78 G, Table 2),[5] and moreover, the mean a(H,NCH_3)/a(N) ratio (1.01, Table 2) agrees with an almost planar equilibrium geometry at the nitrogen atoms. Therefore, in the case of $9^{\bullet+}$ the slightly different *N*-methyl proton splittings can be readily understood as a usual result of the dissimilar environment of the *exo* and *endo* methyl groups.



$9^{\bullet+}$



$10^{\bullet+}$

Radical cation $10^{\bullet+}$ assumes an intermediate position between $1^{\bullet+}$ and $9^{\bullet+}$. The difference of its *exo* (3.76 G) and *endo* *N*-methyl proton splittings (2.56 G; ratio 1.5:1) is larger than that of $9^{\bullet+}$ and smaller than that of $1^{\bullet+}$, whereas the mean a(H, NCH_3)/a(N) ratio (0.87, Table 2) of $10^{\bullet+}$ still agrees with an equilibrium geometry at the nitrogens close to planarity. As in case of $1^{\bullet+}$ the cyclovoltammogram of $10^{\bullet+}$ shows a reversible "two-electron" transfer composed of two superimposed one-electron transfer steps,[14] which indicates that most of the molecular reorganization taking place on oxidation occurs in the first oxidation step. Therefore, crystal structures of corresponding dications can afford a rough picture of what the molecular conformation of the radical cations looks like. From both 1^{2+} and 10^{2+}, crystal molecular structures are known.[2,14] The dication 10^{2+} consists of two roughly planar, resonance-stabilized π-electron systems of polymethine type, which are strongly tilted against each other so that the six-membered ring assumes a twist conformation.[14] The nitrogens in 10^{2+} are almost sp^2-hybridized [deviation from the C(1), C(1A, CH_3), C(1B, CH_3) plane 0.09 Å]. The close contact between the *endo* *N*-methyl groups (3.08 Å) is particularly remarkable which is significantly smaller than the sum of their van der Waals radii (~4 Å). The crystal structure of 1^{2+} shows a 2-fold boat conformation, in which C(1) and C(4) are displaced downward and C(1^i) and C(4^i) upward by 0.27 Å out of the C(2), C(3), C(4a), C(2^i), C(3^i), C($4a^i$) plane.[2] Again, the nitrogens are almost sp^2-hybridized [deviation from the C(1), C(1″A, CH_3), C(1″B, CH_3) plane 0.08 Å]. The contact between the *endo* *N*-methyl groups (3.18 Å) is found not to be as close as in 10^{2+}. Therefore, the crystal structures of the dications 1^{2+} and 10^{2+} do not provide any evidence for a sterically enforced close mutual contact of the *endo* *N*-methyl groups in the corresponding radical cations affecting strongly the *N*-methyl proton splitting in the observed order.

At present we see no reasonable explanation for the origin of the significantly different *N*-methyl proton splittings in $1^{\bullet+}$, which , in our view, cannot be explained conventionally by considering only the different environments of the *N*-methyl groups.

Experimental Section

General. UV–vis spectra were taken on a Cary 17 (Varian). ^1H NMR spectra were recorded on a Bruker AM 500 or a HX 360 spectrometer for [$(CD_3)_2SO$] solutions at room temperature unless otherwise stated. Chemical shifts are reported as δ values with tetramethylsilane as internal standard. *J* values are in Hz. Mass spectra were taken on a Dupont CEC 21-492 or on a Finnigan MAT 212 mass spec-

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trometer (ionization energy 70 eV). To monitor the progress of reactions and the separation of products, TLC (Macherey-Nagel Polygram SIL G/UV_{254} and ALOX N/UV_{254}) was used.

Cyclic voltammetry studies were carried out on degassed acetonitrile[15] solutions containing the sample (0.2–0.8 mM) and tetrabutylammonium perchlorate (0.1 M) at 298 K. The cyclic voltammograms of these solutions were obtained using the scanning potentiostat PAR 262 of EG & G Princeton Applied Research attached to an electrochemical cell which consisted of a "glassy carbon electrode" as working electrode, a standard Ag/AgCl reference electrode, and a platinum counter electrode. Cyclic voltammograms were scanned at a current of 0.1–0.5 mA and a sweep rate of about 100 mV s^{-1}. Redox potentials are referred to ferrocene (Fc, E = 0.352 V) set to 0; Fc/Fc^+ = 0.00 V.

EPR and ENDOR spectra were recorded on a Bruker ESP 300 spectrometer equipped with the ER 252 (ENMR) ENDOR system; g-values were determined by using a NMR gaussmeter and the Hewlett-Packard 5342A microwave frequency counter. This was calibrated with the perylene radical cation. Hyperfine coupling constants measured in megahertz (ENDOR) were converted into gauss using 1 MHz = (0.7145/g) G.

1,3-Dimethyl-6,7-dinitro-1*H*-perimidin-2(3*H*)-one (5).[1] To a vigorously stirred suspension of 1,3-dimethyl-1*H*-perimidin-2(3*H*)-one[16] (6.4 g, 30 mmol) in acetic acid (250 mL) kept below 30 °C by external cooling was added a solution of nitric acid (65%) (25 mL) in acetic acid (20 mL) over a period of 10 min, and stirring was continued for 1 h. The precipitated product was collected and recrystallized from acetic acid to give compound **5** (3.0 g, 33% yield; R_f = 0.5, SIL, ethyl acetate) as yellow crystals: dec above 310 °C; ^{1}H NMR δ 3.55 (6H, s, CH_3), 7.17 (2H, d, J = 9.0 Hz, 4-, 9-H), 8.48 (2H, d, 5-, 8-H); irradiation of NCH_3 (δ 3.55) yielded a strong NOE response for 4-, 9-H (δ 7.17); MS m/z (rel intensity) 302 ($M^{\bullet+}$) (37), 256 (22), 240 (14), 226 (100), 210 (17), 198 (18), 169 (12). Anal. Calcd for $C_{13}H_{10}N_4O_5$: C, 51.66; H, 3.34; N, 18.54. Found: C, 51.79; H, 3.26; N, 18.46.

6,7-Diamino-1,3-dimethyl-1*H*-perimidin-2(3*H*)-one (6). A suspension of **5** (2.42 g, 8 mmol) in dimethylformamide (250 mL) was hydrogenated (*ca.* 1200 mL hydrogen, 48 mmol) in the presence of Pd (5% on charcoal, 200 mg). Then the mixture was heated to about 50 °C to dissolve the precipitated product and was filtered under argon. The filtrate was concentrated at 30 °C under reduced pressure (0.01 mbar) to *ca.* 50 mL. The precipitated product was collected to yield compound **6** (1.30 g, 67% yield; R_f = 0.5, ALOX, ethyl acetate) as brownish crystals: mp 316 °C dec (closed capillary tube); ^{1}H NMR δ 3.21 (6H, s, CH_3), 5.14 (4H, s, NH_2), 6.41 (2H, d, J = 8.2 Hz, 4-, 9-H), 6.58 (2H, d, 5-, 8-H); irradiation of NCH_3 (δ 3.21) yielded a strong NOE response for 4-, 9-H (δ 6.41); MS m/z (rel intensity) 242 ($M^{\bullet+}$) (100), 227 (23), 199 (20), 184 (15), 121 (M^{2+}) (12), 99.5 (199^{2+}) (12). Anal. Calcd for $C_{13}H_{14}N_4O$: C, 64.45; H, 5.82; N, 23.13. Found: C, 64.40; H, 5.73; N, 22.95.

6,7-Bis[(ethoxycarbonyl)amino]-1,3-dimethyl-1*H*-perimidin-2(3*H*)-one (7). A suspension of **5** (4.84 g, 16 mmol) in dimethylformamide (500 mL) was hydrogenated in the presence of Pd (5% on charcoal, 300 mg) as described above. To the filtrate was added diethyl dicarbonate (14.7 mL, 100 mmol), and the reaction mixture was stirred at 80 °C for 2 h. After cooling and adding of dichloromethane to complete precipitation the product was collected. Recrystallization from dimethylformamide afforded compound **7** (4.1 g, 66% yield; R_f = 0.57, ALOX, ethyl acetate) as colorless crystals: dec above 225 °C; ^{1}H NMR δ 1.21 (6H, t, J = 7.0 Hz, CH_3), 3.36 (6H, s, NCH_3), 4.05 (4H, q, CH_2), 6.75 (2H, d, J = 8.2 Hz, 4-, 9-H), 7.37 (2H, d, 5-, 8-H), 8.73 (2H, s, NH); irradiation of NCH_3 (δ 3.36) yielded a strong NOE response for 4-, 9-H (δ 6.75); MS m/z (rel intensity) 386 ($M^{\bullet+}$) (5), 340 (56), 268 (100), 253 (6), 225 (6), 223 (10). Anal. Calcd for $C_{19}H_{22}N_4O_5$: C, 59.06; H, 5.74; N, 14.50. Found: C, 59.21; H, 5.76; N, 14.49.

6,7-Bis[(ethoxycarbonyl)methylamino]-1,3-dimethyl-1*H*-perimidin-2(3*H*)-one (8). A mixture of compound **7** (2.01 g, 5.2 mmol), methyl iodide (20 mL, 0.32 mol), water (1 mL), and powdered barium oxide (20 g) in dimethylformamide (250 mL) was vigorously stirred at ambient temparature for 12 h. The inorganic material was separated by centrifuging and washed with dichloromethane (ca. 100 mL). The combined solutions were washed twice with 2 M hydrochloric acid (ca. 100 mL) and then repeatedly with water, dried ($MgSO_4$), and evaporated. The crude product remaining was chromatographed (silica gel, eluent dichloromethane followed by ethyl acetate) to give compound **8** (1.00 g, 47% yield; R_f = 0.4, SIL, ethyl acetate) as colorless crystals from ethanol–pentane: mp 215–216 °C; ^{1}H NMR δ 0.92–1.28 (6H, m), 2.99–3.09 (6H, m), 3.39 (6H, s), 3.89–4.11 (4H, m), 6.81 (2H, d), 7.35–7.39 (2H, m); MS m/z (rel intensity) 414 ($M^{\bullet+}$) (100), 296 (31), 283 (12), 268 (24), 267 (10), 254 (15), 253 (27), 252 (25), 238 (14), 209 (14). Anal. Calcd for $C_{21}H_{26}N_4O_5$: C, 60.86; H, 6.32; N, 13.52. Found: C, 61.11; H, 6.55; N, 13.63.

3,8-Dihydro-1,3,6,8-tetramethylpyrimido[4,5,6-*gh*]perimidine-2,7(1*H*,6*H*)-dione (2). Compound **8** (2 × 0.50 g, 2.4 mmol) was pyrolized in a pyrolysis apparatus (tube-length 80 cm, diameter 3 cm) at 700 °C/0.001 mbar (temperature of the evaporation zone 200–250 °C, evaporation period *ca.* 3 h). The combined pyrolysates dissolved in dichloromethane were chromatographed [alumina (Brockmann) with ethyl acetate–acetone (1:1)] to give compound **8** (100 mg, 14% yield; R_f = 0.32, SIL, ethyl acetate) as brownish needles from toluene: dec above 250 °C; UV–vis λ_{max}/nm (log ϵ) (ethanol) 398 (3.99), 378 (3.94), 345 (4.10), 332 sh (4.04), 215 (4.85); ^{1}H NMR δ 3.22 (12H, s, CH_3), 6.57 (4H, s, 4-, 5-, 9-, 10-H); MS m/z (rel intensity) 296 ($M^{\bullet+}$) (100), 281 (21), 253 (15), 148 (15). Anal. Calcd for $C_{16}H_{16}N_4O_2$: C, 64.85; H, 5.45; N, 18.91. Found: C, 65.08; H, 5.30; N, 18.69.

1,2,3,6,7,8-Hexahydro-1,3,6,8-tetramethylpyrimido[4,5,6-*gh*]perimidine (3). In a Soxhlet apparatus compound **2** (130 mg, 0.44 mmol) was extracted into a suspension of lithium aluminum hydride (500 mg, 13 mmol) in dry tetrahydrofuran (50 mL) over a period of *ca.* 3 h. After addition of water (0.5 mL) the reaction mixture was separated between saturated aqueous potassium sodium tartrate (200 mL) and dichloromethane and the aqueous phase was repeatedly extracted with dichloromethane (3 × 20 mL). The combined organic layers were concentrated under reduced pressure to 20 mL and chromatographed on alumina (Brockmann) with ethyl acetate–dichloromethane (1:2.5 increasing to 1:1.7) as eluent to give compound **3** (40 mg, 36% yield; R_f = 0.63, ALOX, ethyl acetate) as yellow needles from ethanol: mp 214 °C dec; UV–vis λ_{max}/nm (log ϵ) (ethanol) 368 (4.04), 350 (4.05), 224 (4.45); ^{1}H NMR δ 2.81 (12H, s, CH_3), 3.91 (4H, s, CH_2), 6.47 (4H, s, 4-, 5-, 9-, 10-H); ^{13}C NMR [$(CD_3)_2CO$; 126 MHz] δ 37.7, 72.3, 106.2, 117.3, 138.4; MS m/z (rel intensity) 268 ($M^{\bullet+}$) (100), 267 (22), 253 (27), 252 (46), 238 (59), 237 (26), 208 (13), 207 (12), 133 (14), 126 (15), 118 (14). Anal. Calcd for $C_{16}H_{20}N_4$: C, 71.61; H, 7.53; N, 20.88. Found: C, 71.55; H, 7.67; N, 20.88.

[2,2,7,7-$^2H_4$]-1,2,3,6,7,8-Hexahydro-1,3,6,8-tetramethylpyrimido[4,5,6-*gh*]perimidine (3D). Prepared from compound **2** (100 mg, 0.35 mmol) as described above using lithium aluminum deuteride as reducing agent: compound **3D** (37 mg, 40% yield) had mp 216 °C dec; ^{1}H NMR δ 2.81 (12H, s, CH_3), 6.47 (4H, s, 4-, 5-, 9-, 10-H); MS m/z (rel intensity) 272 ($M^{\bullet+}$) (100), 271 (20), 270 (14), 257 (16), 256 (12), 255 (35), 242 (41), 241 (16), 240 (21), 227 (11), 137 (10), 125 (13), 111 (16), 97 (15). Anal. Calcd for $C_{16}H_{16}D_4N_4$: C, 70.55; H + D, 8.88; N, 20.57. Found: C, 70.74; H + D, 9.07; N, 20.57.

3,6,7,8-Tetrahydro-1,3,6,8-tetramethylpyrimido[4,5,6-*gh*]perimidin-2(1*H*)-one (4). To a solution of compound **6** (1.41 g, 5.8 mmol) in acetonitrile (200 mL) was added sodium cyanoborohydride (5.1 g, 81.6 mmol). Then at the same time (the mixture should remain neutral or slightly acidic) aqueous formaldehyde (37%, 20 mL, 0.25 mol) and acetic acid (15 mL) were slowly added with stirring. The reaction mixture was stirred for an additional 12 h and was then evaporated. To the residue concentrated aqueous sodium hydroxide was carefully added until the gas generation ceased. The reaction mixture was separated between water and dichloromethane. The organic layer was concentrated under reduced pressure

(15) Purified according to: Kiesele, H. *Anal. Chem.* **1980**, *52*, 2230.
(16) Christmann, O. *Chem. Ber.* **1965**, *98*, 1282. See also: Pozharskii, A. F.; Kashparov, I. S. *Khim. Geterotsikl. Soedin.* **1972**, 860.

to 20 mL and purified by filtering through a short silica gel column using dichloromethane–ethyl acetate (5:1) as eluent. On evaporation the residue was chromatographed on alumina (Brockmann) using dichloromethane followed by dichloromethane–ethyl acetate (10:1) as eluent to give compound **4** (33 mg, 2% yield; R_f = 0.45, SIL, ethyl acetate, R_f = 0.18, ALOX, dichloromethane) as yellow crystals from toluene: dec above 250 °C; UV–vis λ_{max}/nm (log ϵ) (ethanol) 389 (3.79), 373 (3.86), 346 (4.01), 228 (4.52); ^{1}H NMR δ 2.85 (6H, s, 6-, 8-NCH_3), 3.26 (6H, s, 1-, 3-NCH_3), 3.99 (2H, s, CH_2), 6.52 (2H, d, J = 8.0 Hz, 5-, 9-H), 6.58 (2H, d, 4-, 10-H); irradiation of 1-, 3-NCH_3 (δ 3.26) yielded a strong NOE response for 4-, 10-H (δ 6.58), irradiation of 6-, 8-NCH_3 (δ 2.85) yielded a strong NOE response for 5-, 9-H (δ 6.52); MS *m/z* (rel intensity) 282 ($M^{\bullet+}$) (100), 281 (39), 280 (29), 267 (23), 266 (51), 265 (25), 253 (14), 252 (36), 251 (75), 238 (16), 237 (13), 236 (11), 223 (11), 222 (11), 221 (24), 83 (10). Anal. Calcd for $C_{16}H_{18}N_4O$: C, 68.06; H, 6.44 N, 19.85. Found: C, 68.30; H, 6.67; N, 19.80.

JO942167E