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Structural and Chemical Properties of 3,10-Diaza-*N*,*N*-dimethyldispiro[5.0.5.3]pentadeca-1,4,8,11-tetraene: A Novel Heterocyclic Dispiro Compound

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The pyridinyl diradicals of the type Py$^\bullet$−(CH$_2$)$_n$−Py$^\bullet$ ($n = 2-4$) are suitable chemical species to obtain information regarding intramolecular spin−spin interactions between two π-radical moieties in a molecule.[1−3] In such pyridinyl diradicals, for instance, 1,1′-(1,3-propanediyl)-bis(pyridinyl) diradical (**1**) is shown to exist as cyclomers of meso (**2a**) and *dl* (**2b**) forms formed by intramolecular cyclization in solution. Of special interest is the experimental fact that the meso form is isomerized thermally into the *dl* form, which is converted photochemically into the meso form. It is also shown that both cyclomers are dissociated by light irradiation under a vacuum of 10^{-6} Torr and exhibit strong dipole−dipole interactions due to a triplet diradical generated by photodissociation at −196 °C. These facts indicate that the cyclomers are important starting materials for the production of diradicals. In this connection, it is noted that the cyclomers provide structurally ideal possibilities for the occurrence of through-bond interactions between two formally separated π systems involved in each dihydropyridine ring. To establish the chemistry of cyclomers through systematic studies of the physicochemical properties, it is desirable to prepare analogous cyclomers by reduction of the corresponding pyridinium salts. In the present paper, we report that reduction of 4,4′-(1,3-propanediyl)-bis(*N*-methylpyridinium) dibromide (**3**) leads to the formation of 3,10-diaza-*N*,*N*-dimethyldispiro[5.0.5.3]pentadeca-1,4,8,11-tetraene (**5**), a novel heterocyclic dispiro compound. Further, we present some characteristic properties of **5** from both experimental and theoretical viewpoints.

Results and Discussion

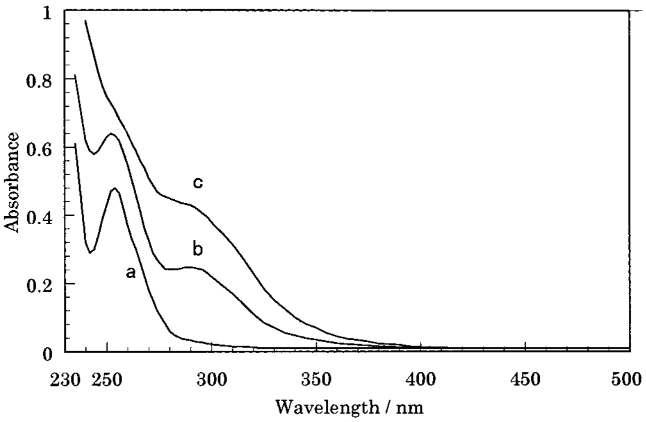

Figure 1. Absorption spectral change during the course of reduction of **3** (8.24×10^{-3} mmol) with 2.8% sodium amalgam (2.47×10^{-2} mmol) in CH$_3$CN (7 mL) at 0 °C: (a) before reduction, (b) after 30 min, and (c) after 10 h.

Preparation and Characterization of 5. Reduction of **3** with sodium amalgam was carried out by two procedures: (P-1) By means of standard vacuum line techniques, **3** (7.7×10^{-2} mmol) and 2.8% sodium amalgam (0.23 mmol) were stirred in a flask at 0 °C for 10 h. After the amalgam changed into a liquid state, the solvent was removed, the residue was extracted with hexane, and then the solvent was replaced by CH$_3$CN or CD$_3$CN for spectral measurements. (P-2) A solution of **3** (0.26 mmol) in water (10 mL) was added dropwise to a suspension of 2.8% sodium amalgam (1.2 mmol) in hexane (50 mL) with stirring for 1 h at 0 °C under nitrogen atmosphere. The organic layer was dried over anhydrous magnesium sulfate and filtered, and then the solvent was replaced by CH$_3$CN or CD$_3$CN in vacuo for spectral measurements. Sampling for spectral measurements was performed under vacuum without isolation of the product.

The reduction process was followed by means of UV−vis absorption spectroscopy. Figure 1 shows the spectral change during the course of reduction by P-1, where the spectral line (a) corresponds to the spectrum of **3**. After about 1 h of reduction, the spectrum changed into the spectral line (b), with the longest wavelength absorption band at about 290 nm. After about 10 h of reduction, the spectrum changed into the spectral line (c), with structureless bands in comparison with the ones observed in the spectra (a) and (b). At this stage, no spectral change was observed upon further reduction. It was noteworthy that no ESR signal was observed at all during the reduction process. In this connection, it is also noted that during electrolytic reduction of **3** in CH$_3$CN, using tetrabuthylammonium perchlorate as supporting electrolyte, no ESR signal due to the intermediate cation radical from **3** was observed. This suggests that **3** undergoes a relatively fast two-electron reduction to give a product (Scheme 1). It is noted that reduction of **3** by P-1 and P-2 yields the same diamagnetic product in almost quantitative yield. The ^{1}H NMR spectrum in Figure 2a suggests clearly that the product should have a highly symmetric structure because the spectral features are very simple. The ^{1}H NMR spectral pattern of six-membered ring protons is very similar to that of 4,4′-bis(1,4-dimethyl-1,4-dihydro-

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(1) Ikegami, Y.; Muramatsu, T.; Hanaya, K. *J. Am. Chem. Soc.* **1989**, *111*, 5782.

(2) Muramatsu, T.; Ikegami, Y.; Hanaya, K.; Onodera, S. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1413.

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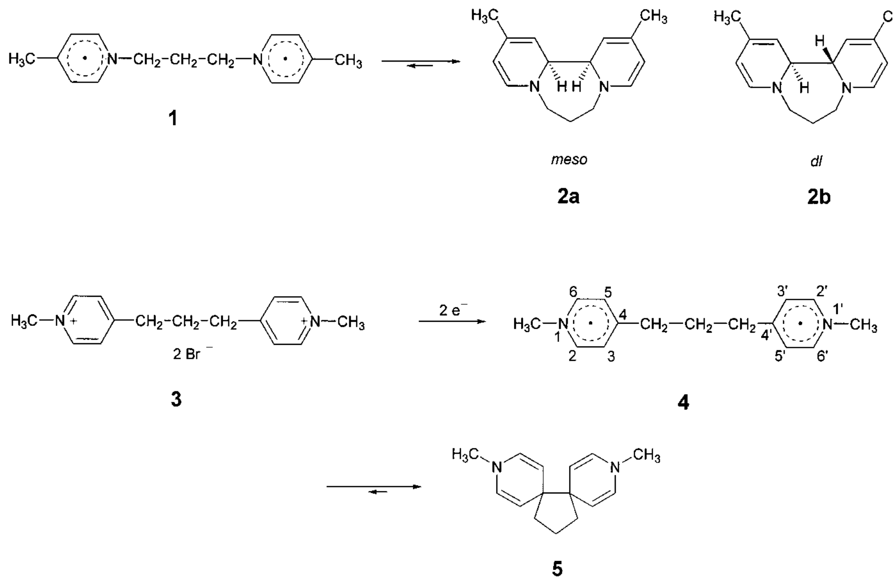
10.1021/jo990514k CCC: $18.00

Scheme 1



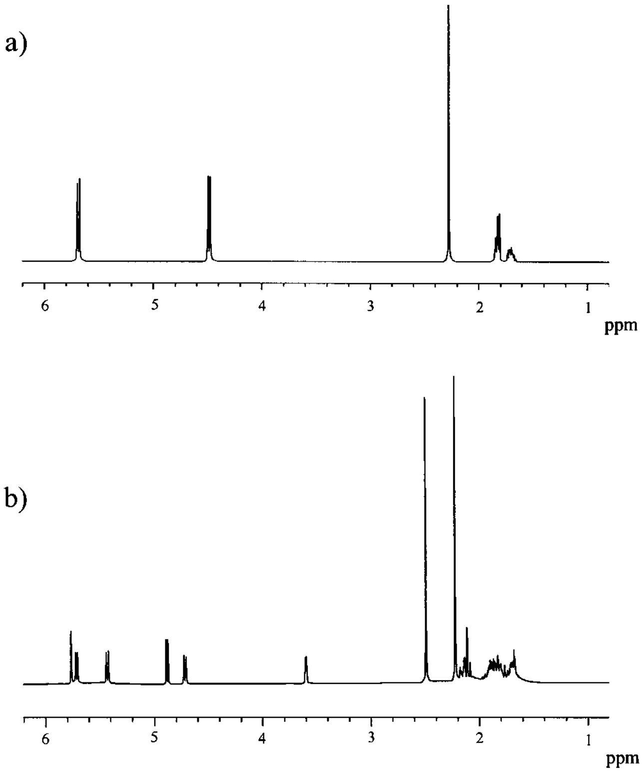
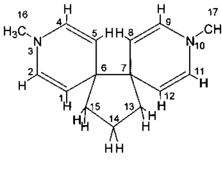


Figure 2. 400 MHz ^{1}H NMR spectra of **5** and **6** in C_6D_6: (a) **5** and (b) **6**, after 40 h of heating of **5** at 160 °C.

Table 1. 400 MHz NMR Spectral Data of 5[a]

		^{1}H NMR		^{13}C NMR
	Position	δ / ppm	J /Hz	δ / ppm
 **5**	1,5,8,12	5.69 (d)	8.1	130.34
	2,4,9,11	4.49 (d)	8.1	103.66
	6,7			51.26
	13,15	1.81-1.85 (m)		42.52
	14	1.68-1.74 (m)		18.75
	16,17	2.28 (s)		39.45

[a] Solvent, benzene-d_6; s, singlet; d, doublet; m, multiplet.

pyridine)[4] [400 MHz ^{1}H NMR (CD_3CN) δ 0.99 (s, 6H), 2.79 (s, 6H), 4.23 (d, $J = 8.3$ Hz, 4H), 5.80 (d, $J = 8.3$ Hz, 4H)], a covalently bonded dimer of 1,4-dimethylpyridinyl radical. Analyses of ^{1}H NMR and ^{13}C NMR spectral data in Table 1 reveal that two dihydropyridine rings are magnetically equivalent with each other and, hence, the molecular structure should belong to the point group C_{2v}. More specifically, the product can be characterized by a cyclopentane ring with vicinal spirocyclic dihydropyridine groups. The assignment of the product was also supported by the mass spectrum, which showed peaks at m/z = 120, 213, and 228 (M^+). Consequently, the reduction product is identified as 3,10-diaza-*N*,*N*-dimethyldispiro-[5.0.5.3]pentadeca-1,4,8,11-tetraene (**5**), a novel heterocyclic dispiro compound.

Chemical Properties of 5. Because **5** is unstable in the presence of oxygen, the chemical properties were studied under degassed conditions. Ultraviolet irradiation shows that **5** exhibits no such response to light as cyclomers **2a** and **2b** do;[2] that is, no ESR signal due to the triplet transition of a two-spin system was observed by irradiation of **5** in 2-methyltetrahydrofuran glass at −196 °C with light of wavelength longer than 290 nm. Further, no NMR spectral change was observed by warming **5** in C_6D_6 up to 100 °C for a long time in the dark. At high temperatures above 150 °C, however, **5** slowly undergoes a thermal isomerization reaction. When a solution of **5** in C_6D_6 was heated at 160 °C for 40 h, the ^{1}H NMR signals characteristic of **5** disappeared and new complex signals attributable to a reaction product were observed (Figure 2b). From a careful examination of the ^{1}H and ^{13}C NMR signals, it was confirmed that the skeleton of the product other than the trimethylene moiety possesses three quaternary C atoms [^{13}C NMR δ 52.9 (sp^3), 63.60 (sp^3), and 111.42 ppm (sp^2)], one secondary C atom [^{1}H NMR δ 2.11 and 2.16 ppm; ^{13}C NMR δ 40.76 ppm (sp^3)], and one tertiary C atom [^{1}H NMR δ 3.60 ppm; ^{13}C NMR 62.38 ppm (sp^3)]. It was further confirmed from the HMQC (600 MHz) measurements and

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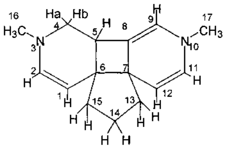
[4] 4,4′-Bis(1,4-dimethyl-1,4-dihydropyridine) was obtained by reduction of 1,4-dimethylpyridinium bromide by method P-1.

Table 2. 400 MHz NMR Spectral Data of 6[a]

		^{1}H NMR		^{13}C NMR
	Position	δ / ppm	J /Hz	δ / ppm
	1	5.42 (dd)	7.3, 1.1	134.14
	2	4.72 (dd)	7.3, 1.8	105.86
	4a	2.16 (dd)	10.6, 1.8	40.76
	4b	2.11 (dd)	10.6, 4.4	
	5	3.60 (dt)	4.4, 1.1	62.38
	6			52.90
	7			63.60
	8			114.42
	9	5.76 (br. t)	1.1	126.44
	11	5.72 (dd)	6.9, 1.1	131.81
6	12	4.88 (d)	6.9	103.66
	13,15	1.65-1.75(m), 1.77-1.91(m)		32.17, 44.21
	14	1.77-1.95(m)		23.19
	16	2.22 (s)		39.18
	17	2.49 (s)		39.46

[a] Solvent, benzene-d_6; s, singlet; d, doublet; dd, double-doublet; t, triplet; m, multiplet.

spin-decoupling techniques that the long-range couplings between H2 and H4b, H1 and H5, H5 and H9, and H9 and H11 were 1.8, 1.1, 1.1, and 1.1 Hz, respectively. These results suggest that the product should possess the structure of 8,12-diaza-*N*,*N*-dimethyltetracyclo[9.3.1.0^{1,5}.0^{5,10}]pentadeca-6,9,13-triene (**6**). In this connection, it is noted that the vicinal coupling constants between H4a and H5 and between H4b and H5 were observed to be 0 and 10.6 Hz, respectively. On the basis of these values, the dihedral angles between H4a and H5 and between H4b and H5 were evaluated to be, respectively, 90° and 40° by using the Karplus relation.[5] These angles were found to be in fairly good agreement with the respective values of 78° and 38° calculated using the geometrical structure of **6** optimized with the semiempirical PM3 method.[6] The mass spectrum shows peaks at m/z = 144, 186, 213, and 228 (M$^+$) and the high mass of the molecular ion peak corresponds to M$^+$ = 228.1629 (elemental formula $C_{15}H_{20}N_2$). This evidence lends further support for the structural assignment for **6**. The spectral data for the assignment of **6** are shown in Table 2. The thermal isomerization reaction from **5** to **6** takes place almost quantitatively at 160 °C. Upon continued heating of **5** for 8 h at higher temperatures of about 200 °C in C_6D_6, however, a mixture of **6** and two other compounds was obtained in the course of thermal reaction, the latter being produced in amounts almost equimolecular with each other. Spectroscopic analyses by means of spin decoupling, 2D measurement, and mass spectrum of the mixture revealed that one is assigned to 1,3-bis(*N*-methyl-1,4-dihydropyridinylidene)propane (**7**) [400 MHz ^{1}H NMR δ 5.67 (dd, J = 7.8 Hz, 2.44 Hz, 2H), 5.50 (dd, J = 7.81 Hz, 2.41 Hz, 2H), 5.42 (dd, J = 7.81 Hz, 1.94 Hz, 2H), 5.24 (dd, J = 7.81 Hz, 1.94 Hz, 2H), 4.57 (t, J = 7.80 Hz, 2H), 2.31 (d, J = 7.80 Hz, 2H), 2.25 (s, 6H) or 2.08 (s, 6H); MS m/z = 211, 226 (M$^+$)] and the other to 1,4′-(1,3-propanediyl)bis(*N*-methyl-1,4-dihydropyridine) (**8**) [400 MHz ^{1}H NMR δ 5.53 (d, J = 7.44 Hz, 4H), 4.51 (dd, J = 7.44 Hz, 3.53 Hz, 4H), 3.31 (m, 2H), 1.7−1.8 (m, 6H), 2.08 (s, 6H) or 2.25(s, 6H); MS m/z = 215, 230 (M$^+$)]. Upon further heating of the solution at 200 °C, the intensities of ^{1}H NMR signals attributed to **7** and **8** were reduced to the same extent and at the same time those attributed to **6** were increased. After heating for a long time, the ^{1}H NMR signals for **7** and **8** disappeared and those for **6** were observed; that is, **6** alone was produced as the final product of the thermal reaction. This suggests that at higher temperatures of about 200 °C the thermal reaction should proceed as follows: First, the opening of the cyclopentane ring takes place at the single bond between two spiro C atoms of **5** to yield diradical **4**. Subsequently, two hydrogen atoms of **4** are eliminated from α-methylene carbons of the trimethylene chain to yield **7**. At the same time, the two hydrogen atoms are added to **4** to produce **8**. In a sense, it may be said that 2 equiv of **4** are in equilibrium with **7** and **8**, where the equilibrium overwhelmingly tends toward the latter. After the formation of **7** and **8**, each of them yields the final product **6** as follows:[7] The former results in the production of **6** through an elimination of two hydrogen atoms and a successive cyclization reaction, and at the same time the latter also results in the production of **6** through an addition of the hydrogen atoms and a successive cyclization reaction (Scheme 2).

As mentioned above, **5** is a stable molecular species in the absence of oxygen. However, **5** slowly undergoes an oxidative decomposition reaction when exposed to air oxygen at room temperature. As the oxidative reactions proceed, an acetonitrile solution of **5** changes gradually from colorless to dark green. At the final stage of oxidation, the main decomposition product was assigned to *N*-methyl-4-pyridone (**9**) from an analysis of the ^{1}H NMR spectrum.[8] With reference to the oxidative decomposition reaction of methyl viologen radical cation presented by Sawyer et al.,[9] the oxidative bond fission between C6 and C7 of **5** was considered to occur slowly to produce a π-diradical. It then follows that the diradical should react with oxygen to yield several unstable dioxetane intermediates, which were readily decomposed to produce mainly **9** and some conjugated aldehydes as the final products.

Structural Properties of 5. To clarify the thermodynamic stability of **5**, we carried out PM3 calculations[6] on **5**, together with cyclomers **10a** and **10b** formed by

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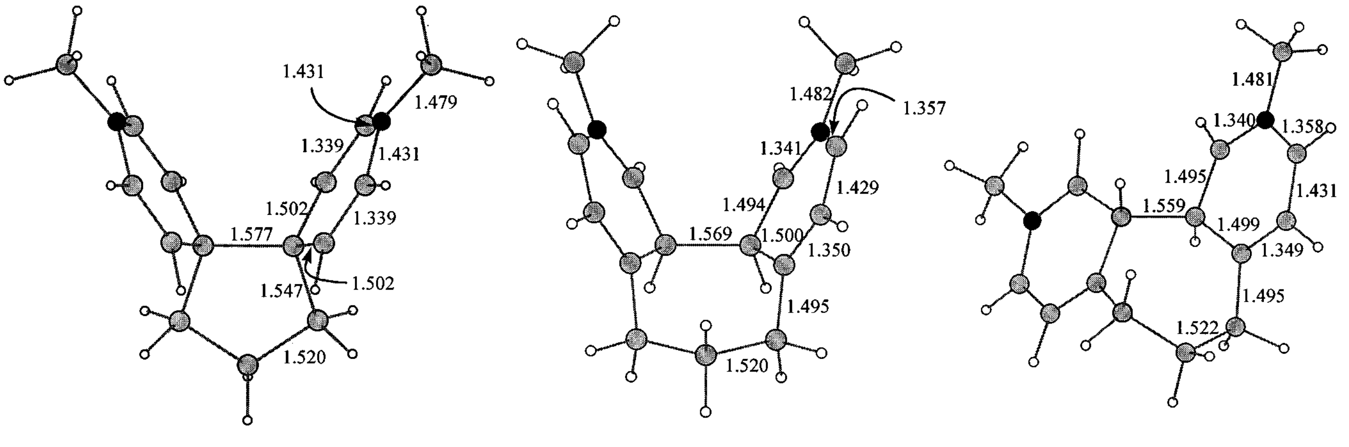
(5) Karplus, M. *J. Am. Chem. Soc.* **1963**, *85*, 2870.

(6) Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 221.

(7) Upon heating at 230 °C, a slight amount of compounds other than **6**−**8** is obtained as the thermal decomposition products of **5.** Since the ^{1}H NMR signals attributed to the decomposition compounds are very low in intensity, overlapped with those of **6**−**8**, no clear assignments were made for them. Because of the appearance of signals attributable to pyridine ring structures at lower fields of δ 8.57 (d) and 6.69 (d), however, the decomposition compounds may be assigned as pyridine derivatives produced by demethylation of **7** and **8**.

(8) That the products consist of several degradation products was confirmed by C8-silica gel reverse-phase TLC, which indicates a large spot with no color and a small spot with dark green. The 400 MHz ^{1}H NMR spectrum arising from the product involved in the firstspot exhibits signals at 7.38 ppm (d, J = 7.6 Hz, 2H), 6.10 ppm (d, J = 7.6 Hz, 2H), and 3.55 ppm (s, 3H) due to *N*-methyl-4-pyridone (**9**), the yield being about 65%. The ^{1}H NMR spectrum arising from products involved in the secondspot exhibits many broad signals over the wide range of chemical shifts (δ 1−8 ppm), but no clear assignments were made for the products. This is because the individual components could not be efficiently isolated in our experimental condition. However, since a broad absorption spectrum is observed around 610 nm, one of the products may be characterized as a species possessing a ring-opened structure with a relatively long conjugated skeleton.

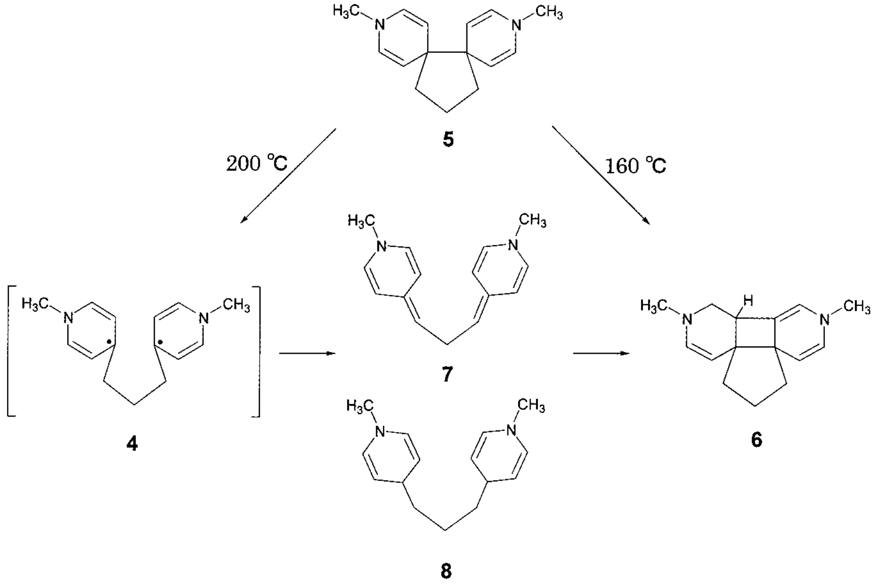
(9) Nanni, E. J., Jr.; Angelis, C. T.; Dickson, J.; Sawyer, D. T. *J. Am. Chem. Soc.* **1981**, *103*, 4268.



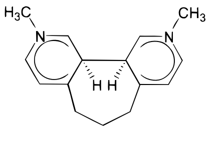
5 : C_{2v} **10a** : C_s **10b** : C_2

Figure 3. Optimized geometrical structures (in Å) of **5**, **10a**, and **10b** by the PM3 method, where N and C atoms are indicated with black and gray circles, respectively.

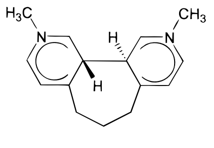
Scheme 2



intramolecular bond formation between C3 and C3′ and between C3 and C5′ of **4**, respectively. The full geometry optimizations led to the prediction that **5** is the most stable in energy among the three isomers. Namely, the heats of formation for **5**, **10a**, and **10b** are calculated to be 58.0, 85.3, and 82.9 kcal/mol, respectively.[10] Evidently, this result provides a good explanation for the production of **5** alone from **3** by two-electron reduction. Interestingly, the optimized C_{2v} geometrical structure of **5** (Figure 3) has a relatively long C−C single bond of ca. 1.58 Å at the position joining directly two dihydropyridine rings in comparison with the other C−C single bonds and those in ordinary saturated hydrocarbons. This aspect in bonding will be reasonably interpreted in terms of a through-bond interaction;[11−13] that is, a perturbational MO analysis reveals that the through-bond interaction is operative between the two nonconjugated C=C−N−C=C moieties with six π electrons via the C−C single bond of interest. It is suggested clearly that the ring-



10a : *meso*



10b : *dl*

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[10] That **10a** and **10b** are less stable than **5** may be ascribed qualitatively to the fact that except for dipolar (ionic) structures no stable Kekulé structure can be written down for the former two and, hence, the contribution of dipolar structures should probably raise the heats of formation.

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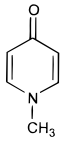
(12) Hoffman, R.; Imamura, A.; Hehre, W. *J. Am. Chem. Soc.* **1968**, *90*, 1499. Gleiter, R. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 696. Dougherty, D. A.; Hounshell, W. D.; Schlegel, H. B.; Bell, R. A.; Mislow, K. *Tetrahedron Lett.* **1976**, 3479.

(13) Toyota, A.; Muramatsu, T.; Koseki, S. *J. Mol. Struct. (THEOCHEM)* **1997**, *393*, 85.

opening reaction observed for the thermal reaction of **5** at higher temperatures above 200 °C should be the consequence of a long C−C single bond at the position joining the two dihydropyridine rings.[11]

Conclusion

The present study shows that the two-electron reduction of **3** with sodium amalgam in vacuo affords **5**, which is characterized by means of NMR, mass, ESR, and UV−vis absorption spectroscopy and that diradical **4** undergoes an intramolecular bond formation between C4 and C4′, leading to the formation of **5**. The primary properties of **5** are summarized as follows: Under degassed conditions, **5** is highly stable for a long time at room temperature. At temperatures higher than 160 °C, **5** shows different behavior in the course of the thermal reactions. Upon heating at 160 °C, **5** undergoes an intramolecular isomerization reaction to give **6**. At higher temperatures above 200 °C, however, **5** undergoes mostly a decomposition reaction to give **7** and **8** and their isomerization reactions then take place respectively to yield **6**. In the presence of oxygen, on the other hand, **5** is unstable even at room temperature. Namely, **5** undergoes a slow oxidative decomposition reaction to give **9** and several degradation products when exposed to air oxygen. The thermal behavior of **5** is accounted for by the theoretical finding that the structure of **5** should exhibit a relatively long C−C single bond at the position joining the two dihydropyridine rings. Finally, it is noted that Bickelhaupt et al.[14] have so far prepared dispiro[2.0.2.3]nona-1,5-diene (**11**) characterized by a cyclopentane ring with vicinal spirocyclic ethylenic systems and, hence, **5** is a higher heterocyclic analogue of **11**.



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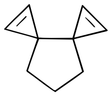

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Experimental Section

General. Standard vacuum line techniques were used in the preparation of **5** and purification of solvents. UV−vis spectra were measured on a Hitachi 220S spectrophotometer and NMR spectra were recorded on a JNM-EX400 NMR spectrometer with residual solvent signal as internal standard. HMQC measurements were carried out on a JNM-LAMBDA 600 NMR spectrometer. Mass spectra were obtained by using a JEOL JMS-DX303 mass spectrometer. To examine the course of reduction spectroscopically, the reaction flask was equipped with a cell for ESR and absorption spectral measurements connected with/through an intervening sintered glass filter. During the reduction, both spectra were measured periodically after filtration.

Material. 4,4′-(1,3-Propanediyl)bis(*N*-methylpyridinium) dibromide (**3**) was prepared by treating 1,3-bis(4-pyridiyl)propane with a large excess of methyl bromide in methanol at 0 °C for about 5 days. The pale yellow solid produced was filtered off, washed with cold methanol, and then recrystalized from methanol to yield colorless crystals: mp 216.5−218.0 °C. Anal. Calcd for $C_{15}H_{20}N_2Br_2$: C, 46.42; H, 5.19; N, 7.22. Found C, 46.53; H, 5.28; N, 7.03.

Solvents. Acetonitrile (Guaranteed Reagent) was passed through an alumina column and distilled. After degassing, the solvent was treated with *N*-methyl-4-(methoxycarbonyl)pyridinyl radical to remove radical-reactive impurities. 2-Methyltetrahydrofuran was refluxed over sodium for 5 days, degassed, and then distilled onto sodium and anthracene in a storage vessel.

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