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Stereochemical reassignment of the isomeric 2,4a,6,8a-tetramethyl-3,4,4a,7,8,8a-hexahydro-<1,5>naphthyridine and 2,5,2′,5′-tetramethyl-5,5′-bi-Δ^1-pyrrolinyl, and of their dioxides

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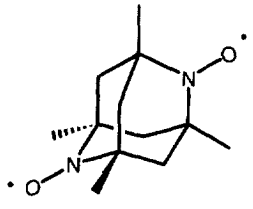
Abstract

The stereochemical relationships between the isomeric 5,6-dimethyl-5,6-dinitrodecane-2,9-diones and their reduction products (the title compounds) have been established.

Keywords: nitrones; nitro compounds; naphthyridines; hexahydropyrrolines; pyrrolines.

Some time ago,[1] a crystalline form[2] of a diazaadamantane nitroxide biradical **1**[3] was reported to be ferromagnetic, with a Curie temperature of 1.48 K, the highest reported for a purely organic, non-ionic ferromagnet. This molecule[3] was designed[4] to obtain an intramolecular ferromagnetic interaction, believed to arise from the presence of degenerate and orthogonal magnetic orbitals in the D_{2d} symmetry of the backbone.[5] It thus could be interesting to obtain the isomeric biradical **2**, of similar globular shape but in which, due to the lower D_2 symmetry, the magnetic orbitals are neither orthogonal nor degenerate. Furthermore, different magnetic crystals, with different intermolecular magnetic interactions, may be expected for the racemic and the enantiomerically pure forms.



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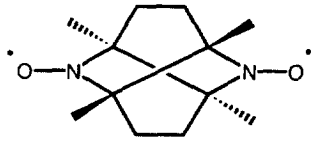

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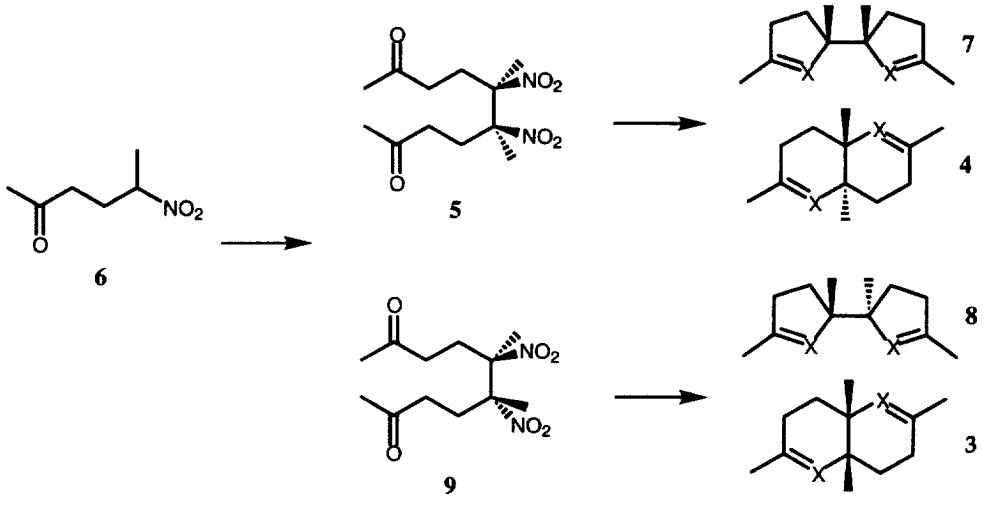
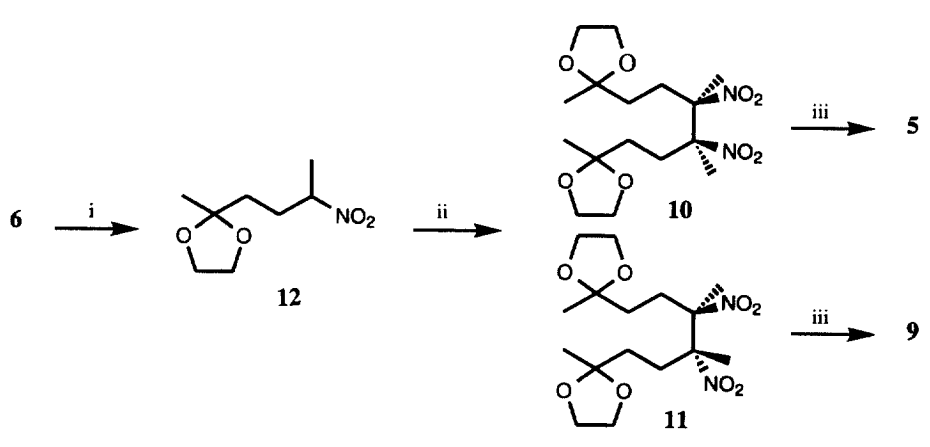
Following Deslongchamps' synthesis of twistane,[6] a suitable precursor could be the chiral dinitrone **3a** (or the diimine **3b**). These molecules had not been previously described. Todd et al.[7] reported in 1959 that they had prepared the *meso* isomer **4a** from **5**, obtained by oxidative dimerization of 5-nitro-2-hexanone **6**. However, the *meso* structures of both **4a** and **5** were only tentative because they were assigned on the basis of the presumed stereochemical course of a Grignard reaction. Reduction of **5** with zinc and ammonium chloride in aqueous ethanol (Scheme 1) was reported to afford a mixture of two isomers **A** and **B** to which structures **7a** and **4a** were assigned. Because of our interest in **3** and also because **3**, **8** or **9** could be precursors of C_2 chiral diamines of recent interest,[8] we have reinvestigated this reaction.



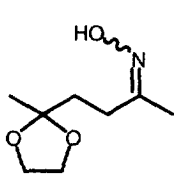
Scheme 1. X=NO: **a**; X=N: **b**

In our hands, the oxidative dimerization of 5-nitro-2-hexanone[9] **6** gave a mixture of **5** and **9**. The first attempts to separate these isomers were unsuccessful, but the mixture of **10** and **11** obtained from the corresponding dioxolane **12** (Scheme 2) was easy to separate: one isomer (mp 138°C) crystallized directly from the reaction mixture. It was resolved into two peaks by chiral HPLC on cellulose acetate[10] and assigned the *dl* structure **11**. After separation by crystallization and/or column chromatography, the dioxolanes **10** and **11**[11] were obtained in 40% and 45% yield, respectively, and converted into the dinitrodiketones **5**[12] (*meso*, mp 110°C, lit.[7] 88°C) and **9**[12] (*dl*, mp 114°C).



Scheme 2. (i) ethylene glycol, PTSA, toluene (90%); (ii) DMF, LiOMe, I_2[13] (85%); (iii) MeOH, H_2SO_4 1 M (95%)

The reduction of these *vic*-dinitro compounds, expected[14] to be rather problematic, was thoroughly investigated. With both **5** and **9**, $LiAlH_4$;[15] Pd/C 10%, H_2;[16] Al/Hg/THF/MeOH/H_2O;[14] Fe, $FeSO_4$, diluted H_2SO_4;[17] CH_3CN/H_2O, $Na_2S_2O_4$, octyl viologen[18] or Zn, NH_4Cl, EtOH/H_2O[19] gave the oxime **13** as the major product. No reaction was observed with Pd/C 10%, $HCOONH_4$[20] or $(NH_4)_2SO_4$, Mg, MeOH/H_2O.[21] Treatment[22] by $NaBH_4$ Pd/C 10% gave a mixture of oxime **13** and alkenes **14**.



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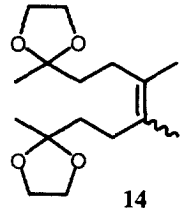

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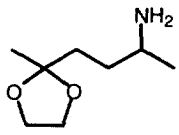

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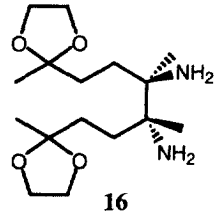

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The reduction[23] of **11** with Sn/HCl 12N led (60% yield) to a 7/93 mixture of isomeric nitrones. The major isomer was crystallized (mp 158°C) from diisopropylether and its *dl* structure **8a**[24] (in accord with the assignment from chiral HPLC) was determined by X-ray crystallography[25]. The crystal (space group $P2_1$) is a conglomerate in which **8a** crystallizes with three water molecules. Reaction with picric acid gave a monopicrate (mp 190°C). The minor isomer **3a** was not obtained in pure form, and was only characterized by NMR spectroscopy.[24]

The reduction of **10** with Sn/HCl 12N led to a single nitrone[26] (mp 202°C), isolated in 43% yield. The crystals obtained were not suitable for X-ray analysis, but as the ^{13}C NMR spectrum was similar to that of **8a** and quite different from that of **3a** (there is no similarity between three ^1H NMR spectra), we assign structure **7a** to this isomer. Reaction with picric acid gave a dipicrate (mp 196°C dec.).

These results suggest that Todd's *meso* bipyrrolinyl dinitrone **A** (mp 150°C, monopicrate 188°C) and *meso* naphthyridine dinitrone **B** (mp 194°C, dipicrate 190°C) were in fact, respectively, **8a** and **7a**.

The diimine **8b** was obtained by reduction of the dinitrone **8a** with Hg/Mg activated by $TiCl_4$.[27] **8b** could also be obtained from **11**: treatment with Mg/Hg activated by $TiCl_4$[28] in presence of *tert*-butanol, yielded the monoamine **15** (25%) and the diamine **16** (55%). The latter was converted with MeOH/H_2SO_4 1 M to a mixture of diimines **3b** (60%) and **8b** (34%).[29] Here again, the naphthyridine methylenes resonated (^{13}C NMR) in a small interval (3.7 ppm) while those of the bipyrrolinyl are spread over 20.4 ppm. This reinforces the previous assignment of structure **7a** to the single dinitrone obtained from **5**.

References

1. (a) Chiarelli, R.; Novak, M.; Rassat, A.; Tholence, J. L. *Nature* **1993**, *363*, 147–149. (b) Chiarelli, R.; Novak, M.; Rassat, A.; Tholence, J. L.; Dromzee, Y.; Jeannin, Y. *Phys. Scr.* **1993**, *T49*, 706–710.
2. Dromzee, Y.; Chiarelli, R.; Gambarelli, S.; Rassat, A. *Acta Cryst.* **1996**, *B C 52*, 474–477.
3. Chiarelli, R.; Rassat, A. *Bull. Soc. Chim. Fr.* **1993**, *130*, 299–303.
4. Rassat, A.; Chiarelli, R. In *Magnetic Molecular Materials*; Gatteschi, D.; Khan, O.; Miller, J. S.; Palacio, F., Eds.; Kluwer Academic Publishers: Dordrecht, 1991; pp. 191–202.
5. Yoshizawa, K.; Hoffmann, R. *J. Am. Chem. Soc.* **1995**, 6921–6926. See also: Chiarelli, R.; Gambarelli, S.; Rassat, A. *Mol. Cryst. Liq. Cryst.* **1997**, *305*, 455–478.
6. Bélanger, A.; Lambert, Y.; Deslongchamps, P. *Can. J. Chem.* **1969**, *47*, 795–802.
7. Brown, R. F. C.; Clark, V. M.; Lamchen, M.; Todd, A. *J. Chem. Soc.* **1959**, 2116–2122.
8. Lucet, D.; Le Gall, T.; Mioskowski, C. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2580–2627.
9. Ballini, R.; Marzioli, P.; Mozzicafredo, A. *J. Org. Chem.* **1996**, *61*, 3209–3211.
10. We thank Professor Mannschreck (University of Regensburg) for this analysis.
11. Compound **10** (*meso*, mp 100°C): ^1H NMR (250 MHz, $CDCl_3$): 1.30 (s, 6H), 1.22–1.43 (m, 2H), 1.56–1.87 (m, 4H), 1.62 (s, 6H), 2.55 (ddd, J=4.1, 4.1, 13.9, 2H), 3.93 (m, 8H); C^{13} NMR (62.9 MHz, $CDCl_3$): 18.8, 23.4, 29.2, 33.5, 64.7, 95.5,

108.8. Compound **11** (*dl*, mp 138°C): ^{1}H NMR (250 MHz, $CDCl_3$): 1.31 (s, 6H), 1.24–1.40 (m, 2H), 1.56 (s, 6H), 1.68 (m, 2H), 2.07 (ddd, J=12.3, 4.7, 17, 2H), 2.57 (ddd, J=3.6, 3.6, 14.8, 2H), 3.92 (m, 8H); ^{13}C NMR (62.9 MHz, $CDCl_3$): 18.5, 23.7, 28.7, 33.4, 64.6, 95.1, 108.8.

12. Compound **5** (*meso*, mp 110°C): ^{1}H NMR (250 MHz, $CDCl_3$): 1.6 (s, 6H), 2.16 (s, 6H), 2.09–2.23 (m, 2H), 2.25–2.5 (m, 4H) 2.6–2.76 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$): 18.8, 28.2, 29.4, 38.0, 95.1, 205.2. Compound **9** (*dl*, mp 114°C): ^{1}H NMR (250 MHz, $CDCl_3$): 1.58 (s, 6H), 2.17 (s, 6H), 2.25–2.58 (m, 6H), 2.62–2.78 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$): 18.5, 28.1, 29.9, 38.0, 94.8, 205.2.
13. Kornblum, N.; Cheng, L. *J. Org. Chem.* **1977**, *42*, 2944–2945.
14. Camps, P.; Font-Bardia, M.; Munoz-Torrero, D.; Solans, X. *Liebigs Annalen* **1995**, 515–522; Camps, P.; Munoz-Torrero, D. *Tetrahedron Lett.* **1994**, *35*, 3187–3190.
15. Wasserman, H. H.; Hearn, M. J.; Haveaux, B.; Thyes, M. *J. Org. Chem.* **1976**, *41*, 153–155.
16. Stevens, R. V.; Lee, A. W. *J. Chem. Soc., Chem. Commun.* **1982**, 102–103.
17. Weis, C. D.; Newkome, G. R. *Synthesis* **1995**, 1053–1065.
18. Park, K.; Oh, C. H.; Sim, W. J. *J. Org. Chem.* **1995**, *60*, 6202–6204.
19. Lamchen, M.; Mittag, T. W. *J. Chem. Soc. (C)* **1966**, 2300–2303; White, D. K.; Greene, F. D. *J. Am. Chem. Soc.* **1978**, *100*, 6760–6761; Gagnon, J. L.; Walters, T. R.; Zajac Jr., W. W. *J. Org. Chem.* **1993**, *58*, 6712–6715.
20. Ram, S.; Ehrenkaufer, R. E. *Tetrahedron Lett.* **1984**, *25*, 3415–3418.
21. Pradjapati, D.; Borah, H. N.; Sander, J. S.; Ghosh, A. C. *Synth. Commun.* **1995**, *25*, 4025–4028.
22. Petrini, M.; Ballini, R.; Rosini, R. G. *Synthesis* **1987**, 713–714.
23. Fukunaga, K.; Kimura, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1107–1111; Asaro, M. F.; Nakayama, I.; Wilson, R. B. *J. Org. Chem.* **1991**, *57*, 778–782.
24. Compound **3a**: ^{1}H NMR (250 MHz, $CDCl_3$): 1.57 (s, 6H), 1.73 (ddd, J=17.8, 11.7, 6.1, 4H), 2.02 (s, 6H), 2.25–2.40 (m, 4H); ^{13}C NMR (62.9 MHz, $CDCl_3$): 19.3, 24.2, 24.6, 26.7, 72.2, 147.2. Compound **8a** (mp 158°C): ^{1}H NMR (250 MHz, $CDCl_3$): 1.59 (s, 6H), 1.90 (s, 6H), 1.94 (m, 2H), 2.30 (s, H_2O), 2.5–2.7 (m, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$): 12.9, 21.6, 27.1, 29.3, 78.8, 144.6.
25. The atomic coordinates for the X-ray structures have been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 124870. We thank Y. Dromzee (University of Paris 6) for this analysis.
26. Compound **7a** (mp 202°C): ^{1}H NMR (250 MHz, $CDCl_3$): 1.45 (s, 6H), 1.88 (m, 2H), 2.06 (s, 6H), 2.55–2.68 (m, 4H), 3.53 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$): 13.2, 20.6, 27.8, 30.4, 78.8, 145.2.
27. Mangeney, P.; Tejero, T.; Alexakis, A.; Grosjean, F.; Normant, J. *Synthesis* **1988**, 255–257.
28. George, J.; Chandrasekaran, S. *Synth. Commun.* **1983**, *13*, 495–499.
29. Compound **3b** : ^{1}H NMR (250 MHz, $CDCl_3$): 1.12 (s, 6H), 1.71–1.76 (m, 4H), 1.87 (s, 6H), 2.09–2.14 (m, 4H); ^{13}C NMR (62.9 MHz, $CDCl_3$): 25.8, 26.6, 27.9, 29.5, 55.2, 167.4. Compound **8b**: ^{1}H NMR (250 MHz, $CDCl_3$): 1.18 (s, 6H), 1.35–1.44 (m, 2H), 1.85 (s, 6H), 2.18–2.27 (m, 2H), 2.38–2.45 (m, 4H); ^{13}C NMR (62.9 MHz, $CDCl_3$): 19.2, 24.0, 31.5, 39.6, 82.2, 172.6.