Asymmetric nitrogen

82.* Tröger base: study of its complex with $HgBr_2$ and its methiodide

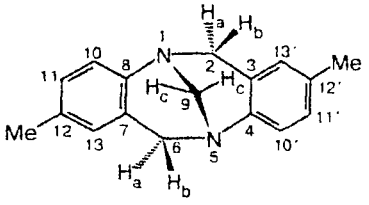
*D. A. Lenev,[a] K. A. Lyssenko,[b] and R. G. Kostyanovsky[c]**

[a]*Higher Chemical College of the Russian Academy of Sciences, 9 Miusskaya pl., 125820 Moscow, Russian Federation. E-mail: lenev@hotmail.com*
[b]*A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 28 ul. Vavilova, 117813 Moscow, Russian Federation. Fax: +7 (095) 135 5085. E-mail: kostya@xray.ineos.ac.ru*
[c]*N. N. Semenov Institute of Chemical Physics, Russian Academy of Sciences, 4 ul. Kosygina, 117977 Moscow, Russian Federation. Fax: +7 (095) 939 2156. E-mail: kost@center.chph.ras.ru*

Reactions of the Tröger base (**1**) with $HgBr_2$ and MeI proceed with the participation of only one N atom. According to the data of X-ray diffraction analysis, the complex $[(\pm)\text{-}\mathbf{1}]_2 \cdot HgBr_2$ crystallizes in the achiral space group *Pn*. Unlike the complex $[(+)\text{-}\mathbf{1}]_2 \cdot HgBr_2$, methiodide of (+)-**1** in MeOH undergoes racemization at 20 °C. The virtual spin-spin coupling constants $^4J_{HH}$ observed for the base (C_2 symmetry) are transformed into the "usual" constants in the case of the desymmetrized methiodide system.

Key words: Tröger base, dibromo-bis(2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocino)mercury(II), X-ray diffraction analysis, n→σ* interaction, Tröger base methiodide, racemization, ^1H and ^{13}C NMR spectra.

The Tröger base (**1**) is the first compound containing three-coordinate asymmetric N atoms; it was resolved into antipodes (by chromatography on lactose[2] and, more recently, on other chiral phases[3–7]). This compound is produced in both enantiomerically pure forms and finds wide application (see the reviews[8,9]).



1

Approximately 50 years elapsed between the synthesis of base **1** (in 1887)[10] and its resolution (in 1944)[2] and determination of the structure (in 1935)[11,12] and then nearly five decades more passed before the absolute configuration was established (X-ray diffraction study; in 1991).[13] The impressive progress in investigations of enantioselective reagents, chiral synthons, and building blocks for supramolecular chemistry based on derivatives and analogs of **1**[5,6,8,9,14–24] gave impetus to studies with the use of their optically active forms. Even over the last two years, the absolute configurations of (*R*,*R*)-(−)-**1** (vibrational CD spectroscopy[14]) and its bis-naphtho- (X-ray diffraction study[15] and CD spectroscopy[16]) and bis-aminoacridine (CD spectroscopy[17]) analogs have been established. Procedures for the preparation of enantiomerically pure Tröger bases are of particular interest. The procedures as yet devised are limited to chromatography on chiral phases[3–7] and five instances of resolution through diastereomeric salts with chiral acids.[13,15,17,23] However, data on their resolution by crystallization with the use of optically active seed crystals (the entrainment procedure) or from optically active solvents with spontaneous resolution are lacking. Conglomerate formation, which has not yet been observed, is the necessary condition for the above-mentioned processes. According to the data of X-ray diffraction studies,[8,9,18,20,21,23–25] compounds of this type crystallize in achiral space groups.

In the present work, we attempted for the first time to search for conglomerates in the series of Tröger bases. For this purpose, we studied the coordination complex $[(\pm)\text{-}\mathbf{1}]_2 \cdot HgBr_2$ (**2**) by X-ray diffraction analysis. In addition, racemization of optically active complex **2** and methiodide **3** was studied. This process is of importance for achieving complete asymmetric transformation (see Ref. 13). The detailed spectral characteristics of compounds **1** and **3** were also obtained.

Experimental

The NMR spectra were recorded on a Bruker WM-400 spectrometer. The optical rotation was measured on a Polamat-A polarimeter. The melting points were determined on a Boetius RNMK-0.5 stage; the rate of heating was 4–5 °C min^{-1}.

Tröger base, 2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (1). The racemate of (±)-**1** was synthe-

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sized according to a known procedure,[19] m.p. 136—137 °C. The enantiomer of (+)-**1** was prepared according to a procedure reported previously,[13] m.p. 130—131 °C, $[\alpha]_D^{21}$ 200.2° (*c* 0.27 MeOH). ^{1}H NMR of (±)-**1** (degassed $CDCl_3$), δ: 2.19 (s, 6 H, 2 Me); 4.11 (dt, 2 H, 2 H_a, $^2J_{a,b}$ = −16.5 Hz, $^4J_{a,c}$ = 1.3 Hz); 4.30 (t, 2 H, 2 H_c, $^4J_{c,a}$ = 1.3 Hz); 4.65 (d, 2 H, 2 H_b, $^2J_{b,a}$ = −16.5 Hz); 6.71 (d, 2 H, H(13), H(13′), $^4J_{13,11}$ = 1.8 Hz); 6.96 (dd, 2 H, H(11), H(11′), $^3J_{11,10}$ = 7.9 Hz, $^4J_{11,13}$ = 1.8 Hz); 7.02 (d, 2 H, H(10), H(10′), $^3J_{10,11}$ = 7.9 Hz). ^{13}C NMR ($CDCl_3$), δ: 20.56 (qt, Me, ^1J = 126.4 Hz, ^3J = 4.4 Hz); 58.45 (tdt, C(2), ^1J = 138.8 Hz, $^3J_{H(13')}$ = 4.4 Hz, $^3J_{H_c}$ = 4.4 Hz); 66.79 (tt, C(9), ^1J = 150.4 Hz, $^3J_{H_a}$ = 7.3 Hz); 124.5 (d, C(10), ^1J = 157.0 Hz); 126.97 (br.d, C(13), ^1J = 152.6 Hz); 127.26 (quint., C(7), ^2J = 5.2 Hz); 127.8 (dqd, C(11), ^1J = 157.0 Hz, $^3J_{Me}$ = 4.4 Hz, $^3J_{H(13)}$ = 7.3 Hz); 132.97 (dq, C(12), $^3J_{H(10)}$ = 6.5 Hz, $^2J_{Me}$ = 6.5 Hz); 145.26 (br.s, C(8)).

Dibromo-bis(2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocino)mercury(II), [(±)-1]$_2$ · $HgBr_2$ (2). A solution of (±)-**1** (100 mg, 0.4 mmol) in EtOH (2 mL) was added dropwise to a solution of $HgBr_2$ (288 mg, 0.8 mmol) in EtOH (1.5 mL) at 60—70 °C. Pale-yellow needle-like crystals of complex **2** precipitated from the transparent solution upon cooling to 25 °C. After recrystallization from EtOH, product **2** was obtained in a yield of 114 mg (66%), m.p. 178—179 °C (lit. data[27]: 173 °C).

The ^{1}H NMR spectra of compounds **2** and **1** in CD_3OD are virtually identical.

Methiodide of (±)-1, 2,5,8-trimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocinium iodide (3). A mixture of (+)-**1** (11.4 mg) and MeI (0.3 mL) in MeOH (2 mL) was kept at 20 °C for 7 days, after which the solution completely lost the optical activity. The solution was concentrated *in vacuo* and product **3** was obtained as a yellow oil (*cf.* lit. data[24]) in a yield of 17.7 mg (100%). ^{1}H NMR ($CDCl_3$), δ: 2.20 (s, 3 H, Me′); 2.24 (s, 3 H, Me); 4.14 (s, 3 H, MeN); 4.19 (dd, 1 H, H_a, $^2J_{a,b}$ = −17.1 Hz, $^4J_{a,c}$ = 2.0 Hz); 4.93 (d, 1 H, H_b, $^2J_{b,a}$ = −17.1 Hz); 5.04 (dd, 1 H, $H_{a'}$, $^2J_{a',b'}$ = −15.4 Hz, $^4J_{a',d}$ = 2.0 Hz); 5.28 (dd, 1 H, H_d, $^2J_{d,c}$ = −11.1 Hz, $^4J_{d,a'}$ = 2.0 Hz); 5.47 (dd, 1 H, H_c, $^2J_{c,d}$ = −11.1 Hz, $^4J_{c,a}$ = 2.0 Hz); 5.77 (d, 1 H, $H_{b'}$, $^2J_{b',a'}$ = −15.4 Hz); 6.84 (br.s, 2 H, H(13), H(13′), Δν = 5.4); 7.13 (ABX spectrum, 2 H, H(11′), H(10′), ^3J = 8.1 Hz, Δν = 9.5, $^4J_{11',13'}$ = 2.0 Hz); 7.24 (dd, 1 H, H(11), $^3J_{11,10}$ = 8.4 Hz, $^4J_{11,13}$ = 2.0 Hz); 8.08 (d, 1 H, H(10), $^3J_{10,11}$ = 8.4 Hz).

X-ray diffraction study. A single crystal of complex **2** suitable for X-ray diffraction study was prepared by crystallization from MeOH at 0 °C. The X-ray diffraction data were collected on an automated four-circle Siemens P3/Pc diffractometer (Mo-Kα radiation (λ = 0.71073), graphite monochromator, θ/2θ scanning technique, 2θ < 60°) at 25 °C. Crystals of $C_{34}H_{36}Br_2HgN_4$ are monoclinic, at 25 °C: a = 10.192(2) Å, b = 11.916(2) Å, c = 13.913(2) Å, β = 110.70(2)°, V = 1580.6(5) Å^3, Z = 2, μ = 7.426 mm^{-1}, $F(000)$ = 836, d_{calc} = 1.809 g cm^{-3}, M = 861.08, space group *Pn*. A total of 4856 reflections were measured, of which 4276 independent reflections were used in subsequent calculations and refinement.

The structure was solved by the direct method and refined anisotropically by the full-matrix least-squares method based on F. The positions of the H atoms were calculated geometrically and refined using the riding model. The absorption correction was applied with the use of the DIFABS program.

The final values of the R factors were as follows: wR_2 = 0.1071 based on all reflections; R_1 = 0.0432 and GOF = 1.010 based on 3642 reflections with $I > 2\sigma(I)$. All calculations were carried out on an IBM PC using the SHELXTL PLUS program package.[26] The structure of complex **2** is shown in Fig. 1.

Results and Discussion

Recently, we have demonstrated[27] that the bidentate ligand 3,3-dimethyldiaziridine, whose N atoms cannot be involved in coordination to the same metal ion, undergoes coordination polymerization with $AgNO_3$ to form homochiral crystals (conglomerate; the space group $P2_12_12_1$). Analogously, we intended to prepare coordination polymers based on compound **1**. Complexes of **1** of different compositions, *viz.*, **1**$_2$ · MX_n,[28] **1** · $(MX_n)_2$,[29] and **1** · MX_n,[25] have been described previously. The X-ray diffraction data were obtained only for **1** · $MeReO_3$ (achiral space group $P2_1/c$).[25]

The composition and the structure of the complex **1**$_2$ · $HgBr_2$ (**2**) were studied by X-ray diffraction analysis (Fig. 1). The geometry of the ligands in complex **2** is virtually identical to that in **1** (*cf.* lit. data[18]). The orientation of the ligands about the Hg atom follows a distorted tetrahedral coordination. The bond angles are 98.7(2)°—133.57(5)°. The dihedral angles between the aromatic rings in ligands **1**′ and **1** (Fig. 1) are 76(1)° and 88(1)°, respectively. The corresponding angles are 92.9 and 97.4° in (±)-**1** and 102.15° in (+)-**1**. According to the data available in the Cambridge Structural Database (CSD), these angles in derivatives of **1** are in the range 88.6—104.01°.

An interesting feature of the crystal structure of **2** is intramolecular stacking between the aromatic rings of the ligands. The angle between the mean planes of the rings is 6° and the distance between their centers is 3.65(2) Å. The distances between the corresponding carbon atoms of the C(11)—C(16) and C(11′)—C(16′)

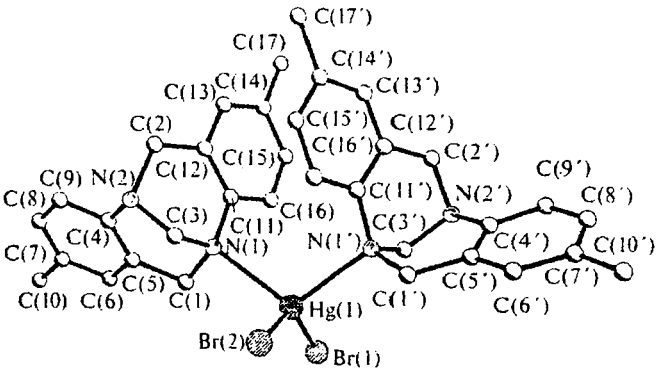


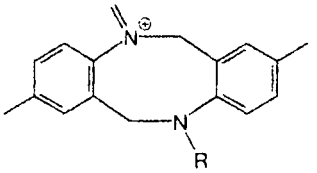
Fig. 1. Overall view of molecule **2** and the atomic numbering scheme.

Selected bond lengths (d/Å) and bond angles (ω):

Bond	d/Å	Angle	ω/deg
Hg(1)—N(1)	2.494(8)	Br(2)—Hg(1)—Br(1)	133.57(5)
Hg(1)—N(1′)	2.462(8)	N(1′)—Hg(1)—N(1)	109.8(3)
Hg(1)—Br(1)	2.502(1)	N(1)—Hg(1)—Br(1)	107.1(2)
Hg(1)—Br(2)	2.494(1)	N(1′)—Hg(1)—Br(1)	100.9(2)
		Br(2)—Hg(1)—N(1)	98.7(2)
		N(1′)—Hg(1)—Br(2)	105.8(2)

Table 1. The N—C bond lengths (Å) in derivatives of **1**

Compound	N(1)—C(3)	N(1)—C(1)	ΔN(1)	N(2)—C(3)	N(2)—C(2)	ΔN(2)
1[18]	1.467	1.458	0.009	1.467	1.458	0.009
2	1.45(1)	1.49(1)	—	1.44(2)	1.46(2)	—
1 · $MeReO_3$ [25]	1.484	1.492	—	1.458	1.473	—
1 · H^+ [13]	1.514	1.506	0.008	1.434	1.496	−0.062
1 · H^+ [20]	1.522	1.506	0.016	1.447	1.466	−0.019
3	1.545	1.493	0.052	1.424	1.464	−0.04



I

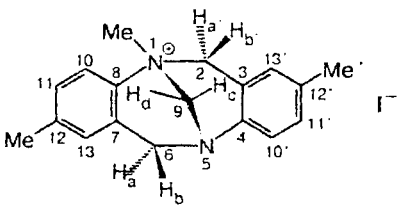
rings are in the range 3.50(2)—3.80(2) Å (hereinafter, the atomic numbering scheme corresponds to that given in Fig. 1).

It appeared that compound **2** crystallized in the achiral space group *Pn* and the expected coordination polymerization was not observed because only one N atom of ligands **1** and **1'** was involved in coordination. One of the possible reasons for this fact is the weakening of the donor ability of the N(2) atom by the anomeric effect (the $n(N)\rightarrow\sigma^*(CN)$ interaction) due to the strictly antiperiplanar orientation of the lone electron pair of the N(2) atom relative to the C(3)—N(1) bond. In derivatives of **1**, this effect is manifested in the elongation of the bond between the C(3) atom and the four-coordinate N(1) atom compared to the N(1)—C(1)(sp^3) bond and in the shortening of the C(3)—N(2) bond compared to the N(2)—C(2)(sp^3) bond (according to the CSD data). The bond lengths and their differences for the most precise structures of a series of derivatives of **1** are given in Table 1. Differences of the same order of magnitude in the bond lengths are observed in the monoprotonated forms and methohalides of 1,3-diaza-5,7-diphenyladmantan-6-one.[30] Apparently, the above-considered stereoelectronic interaction along with steric hindrances and the −I effect of the electron-withdrawing N(1) atom are responsible for hindrances to coordination at the second N(2) atom and methiodide formation in spite of the fact that large excesses of $HgBr_2$ and MeI were used in the syntheses of complex **2** and methiodide **3**, respectively. It should be noted that bis-protonation of compound **1** was indirectly detected only in solutions of concentrated acids.[31]

Yet another important aspect of the chemistry of Tröger bases involves acid-catalyzed[2,8,9,13,17,23,31] and thermal[7] enantiomerization in solutions, which is (along with conglomeration) a necessary condition for complete asymmetric transformation into a single enantiomer.[32] Such diastereomeric transformation of (±)-**1** into (+)-**1** (in 93% yield) under the action of a chiral acid has been performed.[13] It is believed[31] that enantiomerization proceeds according to the dissociation mechanism through an iminium intermediate (**I**, R = H). A similar mechanism was proposed[7] for thermal enantiomerization, which is characterized by a high negative value $\Delta S^{\neq} = -55$ e.u. ($\Delta G^{\neq} = 28.1$ kcal mol^{-1} at 25 °C and $\Delta H^{\neq} = 11.7$ kcal mol^{-1}), typical of heterolytic processes.

The rate of enantiomerization of various derivatives of **1** depends on the Lewis acidity. Actually, compound (+)-**1** is stable to racemization in the presence of a large excess of $HgBr_2$ (refluxing in MeCN for 8 h). At the same time, the complex of (+)-**1** with a stronger Lewis acid, *viz.*, $MeReO_3$, undergoes racemization. This is evident from the following fact: according to the data of X-ray diffraction analysis, the complex described as (5*R*,11*R*)-(+)-**1** · $MeReO_3$ occurs as a racemate.[25] In the cited work, the optical rotation of the complex was not reported and negative results were obtained when this compound was used as a chiral catalyst. However, it is difficult to judge whether racemization occurred in the course of the synthesis (the temperature was below −25 °C) or under conditions of crystallization, which have not been described.[25]

We have found for the first time that methiodide **3** undergoes complete racemization in the course of synthesis from (+)-**1** (1 week at 20 °C). Apparently, racemization proceeds *via* intermediate **I** (R = Me). This observation reveals new possibilities of diastereomeric asymmetric transformations using chiral alkylating reagents or chiral guest molecules upon clathration (see Ref. 24).



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The NMR spectra of compounds **1** and **3** were measured and the assignment of the signals was based on the experimental data on selective double resonance. The observed long-range spin-spin coupling constants (^4J) of the H_a protons with the protons at the C(9) atom correspond to the X-ray diffraction data on the planar W-zigzag conformation of the H_aCNCH_c fragment. Yet another clear example of the transformation of the virtual spin-spin coupling constants $^4J_{HH}$, which are observed in system **1** with symmetry C_2, into the "usual" spin-spin coupling constants in desymmetrized system **3** (see Refs. 33 and 34) was found, the latter constants being twice as large in magnitude as the former constants (Fig. 2). This fact has not been discussed previously.[22,35]

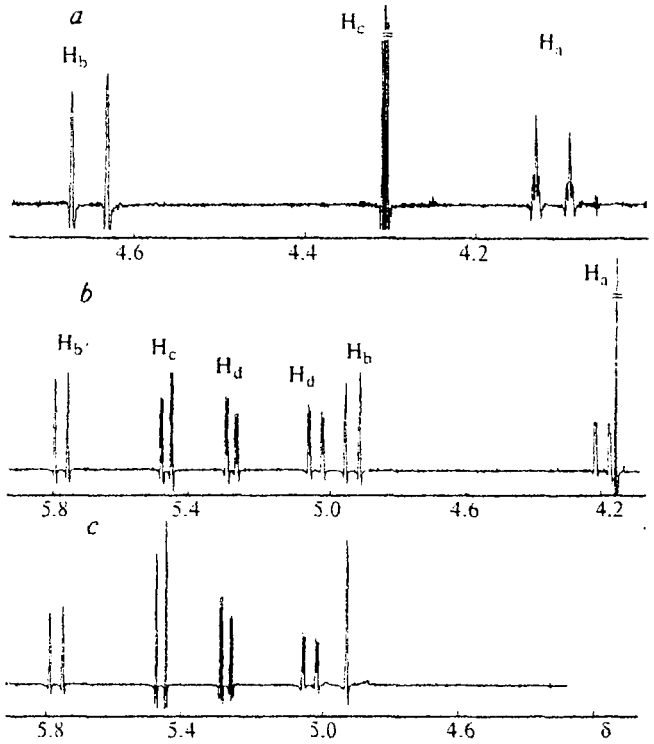

Fig. 2. ^{1}H NMR spectra in the region of signals of the methylene protons measured in the line narrowing mode: *a*, **1** in degassed $CDCl_3$; *b*, **3** in CD_3OD; *c*, **3** in CD_3OD under $\{H_a\}$ conditions.

In conclusion, it should be noted that success was achieved in the search for conglomerates in the series of Tröger bases. We found that in the case of the bis-naphthyl analog of **1**, the melting point of the enantiomer was 45 °C higher (!) than that of the racemate.[15] Currently, we are studying spontaneous resolution of this compound.

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References

1. A. V. Prosyanik, A. I. Mishchenko, O. V. Zelenskaya, A. Forni, I. Moretti, G. Torre, S. Brükner, L. Malpezzi, V. R. Kostyanovsky, and R. G. Kostyanovsky, *Izv. Akad. Nauk, Ser. Khim.*, 1998, 1398 [*Russ. Chem. Bull.*, 1998, **47**, 1359 (Engl. Transl.)].
2. V. Prelog and P. Wieland, *Helv. Chim. Acta*, 1944, **27**, 1127.
3. K. R. Linder and A. Mannschreck, *J. Chromatogr.*, 1980, **193**, 308.
4. K. Saigo, Y. Chen, N. Kubota, K. Tachibana, N. Yonezawa, and M. Hagsegawa, *Chem. Lett.*, 1986, 515.
5. E. Yashima, S. Huang, and Y. Okamoto, *J. Chem. Soc., Chem. Commun*, 1994, 1811.
6. Y. Miyahara, K. Izumi, A. A. Ibrahim, and T. Inazu, *Tetrahedron Lett.*, 1999, **40**, 1705.
7. O. Trapp and V. Schurig, *J. Am. Chem. Soc.*, 2000, **122**, 1424.
8. F. Vögtle, *Fascinating Molecules in Organic Chemistry*, J. Wiley, New York, 1992, Ch. 5, 237.
9. B. G. Bag, *Curr. Sci.*, 1995, **68**, 279.
10. J. Tröger, *J. Prakt. Chem.*, 1887, **36**, 225.
11. M. A. Spielman, *J. Am. Chem. Soc.*, 1935, **57**, 583.
12. E. C. Wagner, *J. Am. Chem. Soc.*, 1935, **57**, 1296.
13. S. H. Wilen, J. Zh. Qi, and P. G. Willard, *J. Org. Chem.*, 1991, **56**, 485.
14. A. Aamouche, F. J. Devlin, and P. J. Stephens, *J. Chem. Soc., Chem. Commun.*, 1999, 361.
15. E. Talas, J. Margitfalvi, D. Machytka, and M. Czugler, *Tetrahedron Asym.*, 1998, **9**, 4151.
16. J. Gawronski and P. Grycz, *Abstr. 7th Int. Conf. on CD, August 25—29*, 1999, Mierki, Poland, P36, p. 90.
17. A. Tatibouet, M. Demeunynck, C. Andraud, A. Collet, and J. Lhomme, *Chem. Commun.*, 1999, 161.
18. C. S. Wilcox, *Tetrahedron Lett.*, 1985, **26**, 5749.
19. R. A. Johnson, R. R. Gorman, R. J. Wnuk, N. J. Crittenden, and J. W. Aiken, *J. Med. Chem.*, 1993, **36**, 3202.
20. J. C. Adrian, Jr., and C. S. Wilcox, *J. Am. Chem. Soc.*, 1989, **111**, 8055.
21. M. J. Crossley, T. W. Hambley, L. J. Mackay, A. C. Try, and R. Walton, *J. Chem. Soc., Chem. Commun.*, 1995, 1077.
22. J. Cudero, P. Jimenez, C. Marcos, C. Pardo, M. Ramos, J. Elguero, and A. Fruchier, *Magn. Res. Chem.*, 1996, **34**, 318.
23. A. Tatibouet, M. Demeunynck, H. Salez, R. Arnaud, J. Lhomme, and C. Courseille, *Bull. Soc. Chim. Fr.*, 1997, **134**, 495.
24. E. Weber, U. Mueller, D. Worsch, F. Vögtle, G. Will, and A. Kirfel, *J. Chem. Soc., Chem. Commun.*, 1985, 1578.
25. W. A. Herrmann, F. E. Kuehn, M. R. Mattner, G. R. J. Artus, M. R. Geisberger, and J. D. G. Correia, *J. Organomet. Chem.*, 1997, **538**, 203.
26. G. M. Sheldrick, SHELXTL PLUS, Version 5, Program for the Refinement of Crystal Structure, Göttingen University, Göttingen (Germany), 1993.
27. R. G. Kostyanovsky, K. A. Lyssenko, and V. R. Kostyanovsky, *Mendeleev Commun.*, 2000, 44.
28. Saeed-ur-Rahman, *J. Chem. Soc. Pak.*, 1987, **9**, 503.
29. Y. Goldberg and H. Alper, *Tetrahedron Lett.*, 1995, **36**, 369.
30. A. V. Goncharov, V. N. Panov, A. V. Maleev, K. A. Potekhin, E. N. Kurkutova, Yu. T. Struchkov, V. A. Palyulin, and N. S. Zefirov, *Dokl. Akad. Nauk SSSR*, 1991, **318**, 907 [*Dokl. Chem.*, 1991 (Engl. Transl.)].
31. A. Greenberg, N. Molinaro, and M. Lang, *J. Org. Chem.*, 1984, **49**, 1127.
32. D. K. Kondepudi, J. Laudadio, and K. Asakura, *J. Am. Chem. Soc.*, 1999, **121**, 1448.
33. R. G. Kostyanovsky, Yu. I. El'natanov, I. I. Chervin, and V. N. Voznesenskii, *Izv. Akad. Nauk, Ser. Khim.*, 1996, 1037 [*Russ. Chem. Bull.*, 1996, **45**, 991 (Engl. Transl.)].
34. R. G. Kostyanovsky, K. A. Lyssenko, D. A. Lenev, Yu. I. El'natanov, O. N. Krutius, and I. A. Bronzova, *Mendeleev Commun.*, 1999, 151.
35. C. Pardo, M. Ramos, A. Fruchier, and J. Elguero, *Magn. Res. Chem.*, 1996, **34**, 708.

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