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# Nickel(II), Copper(II) and Palladium(II) Complexes with Bis-Semicarbazide Hexaazamacrocycles: Redox-Noninnocent Behavior and Catalytic Activity in Oxidation and C–C Coupling Reactions

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for Ni, Cu, and Pd, respectively. The electrochemical behavior of 1-6 was investigated in detail. The electronic structures of 1eoxidized species were studied by EPR, UV-vis-NIR spectroelectrochemistry, and DFT calculations, indicating the redoxnoninnocent behavior of the ligands. Compounds 1-6 were tested in the oxidation of styrene and C-C coupling (Henry and Knoevenagel condensations). Compounds 2 and 5 selectively catalyze the microwave-assisted oxidation of neat styrene to benzaldehyde (up to 88% yield), whereas the 1 and 4 catalytic systems afforded up to 99%  $\beta$ -nitroethanol yield with an appreciable diastereoselectivity toward the formation of the *anti* isomer.

## ■ INTRODUCTION

The ligand-centered reactivity of transition-metal complexes with redox-noninnocent ligands continues to be one of the most exciting topics of coordination chemistry.<sup>1-9</sup> Two IC Forums appeared in the past decade: i.e., on redox-active ligands<sup>10</sup> and on applications of metal complexes with ligandcentered radicals.<sup>11</sup> Base-metal complexes with ligand-centered radicals became of particular interest in multielectron catalysis<sup>12-14</sup> inspired by metalloenzyme systems such as, for example, galactose oxidase, which requires close cooperation between redox-active copper(I/II) with a redox-active phenoxyl/phenolate ligand to catalyze the two-electron oxidation of alcohols to aldehydes,<sup>7.15</sup> attesting to the quick extension of this area of research. These studies attracted considerable attention about 30 years ago and were aimed at an understanding of the electronic structure and bonding of metal complexes with redox-noninnocent ligands and their use in stoichiometric reactions.<sup>16-20</sup> In recent years their use in catalytic reactions has rapidly increased; catalytic functionalization of C-H bonds are well-documented reactions.<sup>21-24</sup> Redox-active ligands can participate in the catalytic transformations by storing and providing electrons, by modifying the Lewis acidity of the metal, and by assisting the formation/ breaking of substrate covalent bond electron transfer events.<sup>13</sup> Cobalt complexes with macrocyclic ligands, namely porphyrins and TAMLH<sub>4</sub> (tetraamido macrocyclic ligand) (Chart 1), were reported to assist in the formation of catalytically competent Fischer-type nitrenes, key intermediates in amination and aziridination of organic substrates, via electron transfers from both the metal and the ligand or via two ligand-to-substrate single-electron-transfer events.<sup>25,26</sup>

The rational design of efficient catalysts for important chemical reactions requires an understanding of their structures and spectroscopic properties, as well as the search for new systems supported by redox-active ligands. Ssubstituted isothiosemicarbazides ( $H_2NNC(SR)NH_2$ ) and isothiosemicarbazones ( $R_1R_2C$ =NNC(SR)NH<sub>2</sub>) are known

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Chart 1. Redox-Noninnocent Macrocyclic Ligands: Tetraphenylporphyrin (Left) and TAMLH<sub>4</sub> (Right)



for their redox-noninnocent properties in metal complexes.<sup>27</sup> A number of nickel(II) complexes with 14-membered macrocycles with two or only one isothiosemicarbazide moiety were prepared via the condensation reaction of pentane-2,4-dione and S-alkylisothiosemicarbazidium iodide by using nickel(II) as a template.<sup>27</sup> The use of isothiosemicarbazides ([H<sub>2</sub>NNHC-(SR)NH<sub>2</sub>]I) as building blocks in template condensation reactions with  $\beta$ -diketones allowed for the stepwise building of macrocycles with a *cis* arrangement of –SR groups (e.g. I),<sup>28,29</sup> as well as macrocycles with a *trans* arrangement of –SR groups (e.g., II) assembled in a single reaction step (Chart 2).<sup>30,31</sup>

Chart 2. Line Drawing of the 14-Membered Hexaazamacrocyclic Nickel(II) Complexes with *cis* and *trans* Arrangements of -SMe Groups



Attempts to obtain metal-free macrocycles by demetalation failed, precluding the investigation of the coordination chemistry of other transition metals with these types of ligands.<sup>27</sup>

Quite recently, some of us developed a stereoselective synthesis of previously unknown 14-membered cyclic bissemicarbazones IX that can be considered as novel potentially redox noninnocent ligands. A key step in the synthesis involved an acid-catalyzed cyclization of the hydrazones of 4-(3-oxobutyl)semicarbazides VII (Scheme 1).<sup>32-34</sup> The semicarbazides VII were prepared via a four-step strategy involving amidoalkylation of the sodium enolate of pentane-2,4-dione with *N*-(tosylmethyl)carbamates IVa to give the products of the tosyl group substitution, compounds Va, followed by a base-promoted retro-Claisen reaction and treatment of the obtained  $\beta$ -carbamato ketones VIa with refluxing hydrazine.

The main disadvantage of this approach was the low isolated yields (29-42%) for substitution of the ethoxy group in VIa by the hydrazine fragment due to the harsh reaction conditions. Subsequently, the synthesis of hydrazones VII was significantly improved by using novel semicarbazone-based amidoalkylation reagents IVb prepared by the three-component condensation of semicarbazones with aldehydes and *p*-toluenesulfinic acid.<sup>35</sup> These reagents were converted in two steps via Vb into VIb, which reacted with excess hydrazine in refluxing EtOH to give VII. All of the above reactions proceeded in excellent yields. During this study, it was found that hydrazones of  $\beta$ -(4semicarbazono)ketones VIII, readily formed by the treatment of VIb with hydrazine under mild conditions, can be also transformed into macrocycles IX by using catalytic amounts of a strong acid. This cyclization is characterized by very high trans selectivity (trans:  $cis \ge 97:3$ ). The developed approach allows for a relatively rapid synthesis of macrocycles IX on a multigram scale. In contrast to reported examples of 14membered macrocycles based on isothiosemicarbazides,<sup>27</sup> isothiocarbazides<sup>36,37</sup> IX are conformationally more flexible, providing a rather dynamic binding cavity. However, their application as ligands in coordination chemistry is hampered by the extremely low solubility of these macrocycles in common solvents, including DMSO, DMF, water, etc. The low solubility can be explained by a high stability of the crystal structure due to strong H-bonding between H-N-C=O

Scheme 1. Two Approaches to 14-Membered Hexaazamacrocycles IX Starting from Ethyl Carbamate IIIa or Aldehyde Semicarbazone IIIb



fragments of different molecules, providing the formation of zigzag polymer-like chains. Clearly, selective alkylation at the hydrazine nitrogen atom of these fragments could result in macrocycles which are expected to be soluble in organic solvents and retain the ability for complex formation.

Herein we describe the synthesis of the two semicarbazidebased racemic 14-membered hexaazamacrocycles  $H_2L^H$  and  $H_2L^{OMe}$  (Chart 3), which are soluble in organic solvents, by

Chart 3. Proligands and Complexes Reported in This Work  $^{a}$ 



<sup>*a*</sup>Underlined compound numbers indicate compounds studied by X-ray crystallography.

selective alkylation of the corresponding unsubstituted precursors IX in Scheme 1 (Ar = Ph, 4-MeOC<sub>6</sub>H<sub>4</sub>) and their nickel(II), copper(II), and palladium(II) complexes 1–6 (Chart 3). In addition, the structure and spectroscopic properties of their 1e-oxidized species are reported. The ability of these complexes to catalyze the microwave-assisted oxidation of neat styrene to benzaldehyde as well as the Henry C–C coupling of benzaldehyde with nitroethane and the ultrasound-assisted Knoevenagel condensation of benzaldehyde and malononitrile was tested, and the results are discussed.

#### EXPERIMENTAL SECTION

Materials and Methods. All starting materials were purchased from Sigma-Aldrich, Acros, and TCI and used as received unless specified otherwise. The racemic macrocycles trans-IX (Ar = Ph, 4- $^{\rm MeOC_6H_4}$ ) were prepared by following the literature proce-dures.  $^{32-35}$  1D ( $^{\rm 1}$ H,  $^{\rm 13}$ C) and 2D ( $^{\rm 1}$ H- $^{\rm 1}$ H COSY,  $^{\rm 1}$ H- $^{\rm 1}$ H TOCSY, <sup>1</sup>H-<sup>1</sup>H NOESY, <sup>1</sup>H-<sup>13</sup>C HSQC, <sup>1</sup>H-<sup>13</sup>C HMBC) NMR spectra of the proligands and their nickel(II) and palladium(II) complexes were measured on Bruker spectrometers (500 and 600 MHz) in DMSO- $d_6$ or CDCl<sub>3</sub> at 25 °C. Chemical shifts are guoted relative to the solvent signals. Atom labeling used in the NMR resonance assignment is shown in Scheme S1. UV-vis absorption spectra were recorded on a PerkinElmer Lambda 650 spectrophotometer. ESI mass spectra were measured on a Bruker Esquire 3000 mass spectrometer by using MeCN-MeOH as the solvent. Infrared spectra were obtained on a Bruker Vertex 70 FT-IR spectrometer by means of the attenuated total reflection technique or on a Bruker Alpha-T spectrometer on KBr pellets. All elemental analyses were performed at the Microanalytical Laboratory of the University of Vienna with a PerkinElmer 2400 CHN Elemental Analyzer.

*trans*-2,9-Dibutyl-7,14-dimethyl-5,12-diphenyl-1,2,4,8,9,11hexaazacyclotetradeca-7,14-diene-3,10-dione ( $H_2L^H$ ). To a mixture of NaH (0.051 g, 2.13 mmol) and macrocycle *trans*-IX (Ar = Ph in Scheme 1) (0.397 g, 0.98 mmol) was added anhydrous DMF (4.2 mL), and the obtained suspension was stirred at room temperature for 5 min. Slow gas evolution was observed, and then butyl iodide (1.097 g, 5.96 mmol) was added in one portion. The

resulted colorless mixture was stirred for 3 h. During the first 1 h the gas evolution faded, the initial precipitate dissolved, and needlelike crystals precipitated. After completion of the reaction, to the obtained suspension were added H<sub>2</sub>O (15 mL) and petroleum ether (10 mL), and the resulting mixture was cooled to 0 °C. The oily precipitate was filtered, and washed with ice-cold  $H_2O$  (6  $\times$  3 mL) and petroleum ether to result in a fine powder, which was washed with cold diethyl ether  $(2 \times 3 \text{ mL})$  and dried to give  $H_2L^H$  (0.447 g, 88%) as a white solid. The analytically pure sample was obtained after crystallization from boiling toluene. Mp: 178-179 °C (toluene). Anal. Calcd for C<sub>30</sub>H<sub>42</sub>N<sub>6</sub>O<sub>2</sub>: C, 69.47; H, 8.16; N, 16.20. Found: C, 69.55; H, 8.25; N, 16.18. IR (KBr):  $\nu_{max}$  3414 br s ( $\nu$ (NH)), 3086 w, 3061 w, 3032 w ( $\nu$ (CH<sub>arom</sub>)), 1661 vs (amide-I), 1636 m ( $\nu$ (C=N)), 1606 w, 1584 w  $(\nu(CC_{arom}))$ , 1510 vs (amide-II), 1059m  $(\nu(N-N))$ , 744 s, 698 s  $(\delta(CH_{arom}))$  cm<sup>-1</sup>. The recorded IR spectrum is shown in Figure S1. <sup>1</sup>H NMR (600.13 MHz, DMSO- $d_6$ ):  $\delta$  7.26–7.31 (2 × 4H, m, CH in two Ar), 7.16–7.19 (2 × 1H, m, CH in two Ar), 7.08 (2 × 1H, d,  ${}^{3}J$  = 8.5 Hz, two NH), 5.05 (2 × 1H, ddd,  ${}^{3}J = 8.5$ ,  ${}^{3}J = 6.4$ ,  ${}^{3}J = 4.6$  Hz, two CH-N), 3.40-3.46 (2 × 1H, m,  $H_A$  in two NCH<sub>A</sub>H<sub>B</sub>), 2.95-3.01 $(2 \times 1H, m, H_B \text{ in two NCH}_A H_B)$ , 2.96  $(2 \times 1H, dd, {}^2J = 16.3, {}^3J =$ 6.4 Hz,  $H_A$  in two  $CH_AH_B$ ), 2.91 (2 × 1H, dd, <sup>2</sup>J = 16.3, <sup>3</sup>J = 4.6 Hz,  $H_{\rm B}$  in two CH<sub>A</sub> $H_{\rm B}$ ), 1.87 (2 × 3H, s, CH<sub>3</sub> in two CH<sub>3</sub>C=N), 0.88-1.14 (2 × 4H, m,  $CH_2$  in two  $CH_2CH_2$ ), 0.71 (2 × 3H, t,  ${}^{3}J$  = 7.3 Hz,  $CH_3$  in two  $CH_2CH_3$ ) (see also Figure S2). <sup>13</sup>C NMR (150.90 MHz, DMSO-d<sub>6</sub>): δ 171.80 (Cq, C=N), 157.76 (Cq, C=O), 143.13 (Cq in Ar), 127.84 (CH in Ar), 126.13 (CH in Ar), 125.91 (CH in Ar), 50.51 (CH-N), 47.23 (NCH<sub>A</sub>H<sub>B</sub>), 43.08 (CH<sub>A</sub>H<sub>B</sub>), 27.86 (CH<sub>2</sub> in CH<sub>2</sub>CH<sub>2</sub>), 19.54 (CH<sub>2</sub> in CH<sub>2</sub>CH<sub>2</sub>), 18.88 (CH<sub>3</sub>C=N), 13.56 (CH<sub>3</sub> in  $CH_2CH_3$ ) (see also Figure S3). The solubility of the compound in DMSO is about 10 mg/mL.

trans-2,9-Dibutyl-7,14-dimethyl-5,12-bis(4-methoxyphenyl)-1,2,4,8,9,11-hexaazacyclotetradeca-7,14-diene-3,10-dione  $(H_2L^{OMe})$ . Method A. The reaction of macrocycle trans-IX (Ar = 4-MeOC<sub>6</sub>H<sub>4</sub> in Scheme 1) (0.430 g, 0.92 mmol) with NaH (0.047 g, 1.96 mmol and butyl iodide (1.029 g, 5.59 mmol) in DMF (4.6 mL) (rt, 3 h) and subsequent workup were performed as described for  $H_2 L^{\rm H}$ . Yield: 0.468 g, 88% of white solid. Mp: 203.5–204.5 °C (toluene). Anal. Calcd for C<sub>32</sub>H<sub>46</sub>N<sub>6</sub>O<sub>4</sub>: C, 66.41; H, 8.01; N, 14.52. Found: C, 66.45; H, 8.15; N, 14.62. IR (KBr):  $\nu_{\text{max}}$  3418 br s, 3370 br sh ( $\nu$ (NH)), 3068 w, 3059 w, 3037 w ( $\nu$ (CH<sub>arom</sub>), 1666 vs (amide-I), 1615 m ( $\nu$ (C=N)), 1584 m ( $\nu$ (CC<sub>arom</sub>)), 1510 vs (amide-II), 1244 s  $(\nu(C-O))$ , 1061 m  $(\nu(N-N))$ , 1032 s  $(\nu(C-O))$ , 836 s, 809 s  $(\delta(CH_{arom}))$  cm<sup>-1</sup>. The full IR spectrum is shown in Figure S4. <sup>1</sup>H NMR (600.13 MHz, DMSO- $d_6$ ):  $\delta$  7.18–7.21 (2 × 2H, m, CH in two Ar), 7.03 (2 × 1H, d,  ${}^{3}J$  = 8.6 Hz, two NH), 6.82–6.86 (2 × 2H, m, CH in two Ar), 5.00 (2 × 1H, ddd,  ${}^{3}J$  = 8.6,  ${}^{3}J$  = 6.4,  ${}^{3}J$  = 4.4 Hz, two CH-N), 3.70 (2  $\times$  3H, s, CH<sub>3</sub> in two OCH<sub>3</sub>), 3.41–3.47 (2  $\times$  1H, m,  $H_A$  in two NCH<sub>A</sub>H<sub>B</sub>), 2.95–3.01 (2 × 1H, m,  $H_B$  in two NCH<sub>A</sub>H<sub>B</sub>), 2.92 (2 × 1H, dd,  ${}^{2}J$  = 16.3,  ${}^{3}J$  = 6.4 Hz,  $H_{\rm A}$  in two  $CH_{\rm A}H_{\rm B}$ ), 2.86 (2 × 1H, dd,  ${}^{2}J = 16.3$ ,  ${}^{3}J = 4.4$  Hz,  $H_{\rm B}$  in two CH<sub>A</sub>H<sub>B</sub>), 1.86 (2 × 3H, s, CH<sub>3</sub> in two CH<sub>3</sub>C=N), 0.88-1.15 (2  $\times$  4H, m, CH<sub>2</sub> in two  $CH_2CH_2$ ), 0.71 (2 × 3H, t, <sup>3</sup>J = 7.3 Hz,  $CH_3$  in two  $CH_2CH_3$ ) (see also Figure S5). <sup>13</sup>C NMR (150.90 MHz, DMSO- $d_{\delta}$ ):  $\delta$  171.67 (Cq, C=N), 157.75 (Cq, C=O), 157.68 (Cq in Ar), 135.00 (Cq in Ar), 126.97 (CH in Ar), 113.24 (CH in Ar), 54.91 (OCH<sub>3</sub>), 49.92 (CH-N), 47.26 (NCH<sub>A</sub>H<sub>B</sub>), 43.12 (CH<sub>A</sub>H<sub>B</sub>), 27.89 (CH<sub>2</sub> in CH<sub>2</sub>CH<sub>2</sub>), 19.58 (CH<sub>2</sub> in CH<sub>2</sub>CH<sub>2</sub>), 18.97 (CH<sub>3</sub>C=N), 13.53 (CH<sub>3</sub> in CH<sub>2</sub>CH<sub>3</sub>) (see also Figure S6). <sup>1</sup>H, <sup>13</sup>C-HSQC, <sup>1</sup>H, <sup>13</sup>C-HMBC and <sup>1</sup>H, <sup>1</sup>H-NOESY spectra are shown in Figures S7-S11, respectively. The solubility of the compound in DMSO is about 10 mg/mL.

Method B.  $H_2L^{OMe}$  (0.668 g, 86%, white solid) was prepared from NaH (0.070 g, 2.91 mmol), macrocycle *trans*-IX (Ar = 4-MeOC<sub>6</sub>H<sub>4</sub> in Scheme 1) (0.626 g, 1.34 mmol) and butyl bromide (1.107 g, 8.08 mmol) in DMF (5 mL) (rt, 3 h) as described for  $H_2L^H$ .

mmol) in DMF (5 mL) (rt, 3 h) as described for  $H_2L^H$ . **Synthesis of Complexes.** *NiL<sup>H</sup>* (1). NiCl<sub>2</sub>·6H<sub>2</sub>O (48 mg, 0.2 mmol) and  $H_2L^H$  (104 mg, 0.2 mmol) in DMF (1.5 mL) were stirred at 95 °C under argon for 3 h. The mixture was cooled to room temperature, and the red crystals that formed were filtered off, washed with water, and dried in vacuo. Yield: 96 mg, 83%. Anal. Calcd for  $C_{30}H_{40}NiN_6O_2$  ( $M_r = 575.37$ ): C, 62.62; H, 7.01; N, 14.61. Found: C,

	CuL <sup>H</sup> ·2EtOH	H <sub>2</sub> L <sup>OMe</sup>	NiL <sup>OMe</sup>	CuL <sup>OMe</sup>	PdL <sup>OMe</sup>
empirical formula	C34H52CuN6O4	$C_{32}H_{46}N_6O_4$	C <sub>32</sub> H <sub>44</sub> NiN <sub>6</sub> O <sub>4</sub>	$C_{32}H_{44}CuN_6O_4$	$C_{32}H_{44}N_6O_4Pd$
fw	672.36	578.75	635.44	640.27	683.13
space group	$P\overline{1}$	Pbca	Pbca	$P2_1/c$	Pbca
a, Å	8.2547(6)	12.46906(5)	12.4254(9)	7.8910(3)	11.1119(3)
b, Å	9.8118(5)	12.46906(5)	12.0463(8)	12.4896(4)	12.5051(3)
c, Å	12.0730(7)	20.80694(13)	20.6886(13)	16.1132(5)	21.8330(6)
$\alpha$ , deg	90.282(3)				
$\beta$ , deg	105.555(3)			102.2179(15)	
γ, deg	113.128(3)				
<i>V</i> , Å <sup>3</sup>	859.57(9)	3235.01(3)	3096.7(4)	1552.07(9)	3033.81(14)
Ζ	1	4	4	2	4
λ, Å	0.71073	1.54184	0.71073	0.71073	0.71073
$ ho_{\rm calcd'}~{\rm g~cm^{-3}}$	1.299	1.188	1.363	1.370	1.496
cryst size, mm <sup>3</sup>	$0.48\times0.40\times0.20$	$0.59 \times 0.33 \times 0.26$	$0.08 \times 0.06 \times 0.01$	$0.15 \times 0.07 \times 0.03$	$0.10 \times 0.08 \times 0.07$
Т, К	100(2)	296(2)	100(2)	100(2)	100(2)
$\mu$ , mm <sup>-1</sup>	0.681	0.638	0.673	0.750	0.660
R1 <sup>a</sup>	0.0417	0.0777	0.0330	0.0509	0.0311
wR2 <sup>b</sup>	0.1208	0.2513	0.0795	0.1078	0.0708
GOF <sup>c</sup>	1.060	1.072	1.028	1.132	1.010
${}^{a}R1 = \sum   F_{a}  -  F_{a}  /$	$\Sigma  F_{\rm ell}  {}^{b} w R2 = \{ \Sigma [w(F_{\rm ell})  w ] \}$	$(2^{2} - F_{2}^{2})^{2} ] / \sum [w(F_{2}^{2})^{2}] $	$^{1/2}$ , <sup>c</sup> GOF = { $\sum [w(F_{1})^{2} + $	$(-F_{1}^{2})^{2}/(n-p)^{1/2}$ , wh	here <i>n</i> is the number of

Table 1. Crystal Data and Details of Data Collection for  $CuL^{H} \cdot 2EtOH$  (2·2EtOH),  $H_2L^{OMe}$ ,  $NiL^{OMe}$  (4),  $CuL^{OMe}$  (5), and  $PdL^{OMe}$  (6)

 ${}^{a}\text{R1} = \sum [|F_{o}| - |F_{c}|| \sum |F_{o}| - w\text{R2} = \{\sum [w(F_{o}^{2} - F_{c}^{2})^{2}] / \sum [w(F_{o}^{2} - F_{c}^{2})^{2}] / (n-p) \}^{1/2}, \text{ where } n \text{ is the number of reflections and } p \text{ is the total number of parameters refined.}$ 

62.65, 62.57; H, 7.09, 7.12; N, 14.53, 14.54. ESI MS (positive ion mode for <sup>58</sup>Ni isotope): m/z 575 [M + H]<sup>+</sup>, 597 [M + Na]<sup>+</sup>. IR (most characteristic bands, cm<sup>-1</sup>): 3407 br, 2956 m, 2929 m, 2871 m, 1639 vs, 1604 vs, 1580 s, 1493 s, 1446 s, 1390 vs, 1360 vs, 1075 s, 766 s, 752 s, 699 vs. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  7.46 (2H, d, J = 6.7Hz,  $H_2 + H_6$ , Ar), 7.31 (2H, t, J = 6.5 Hz,  $H_3 + H_5$ , Ar), 7.20 (1H, t, J= 6.5 Hz, H<sub>4</sub>, Ar), 4.75 (1H, s, CH-N), 3.75 (1H, brs,  $H_A$  in  $NCH_AH_B$ ), 3.18 (1H, d, J = 18.0 Hz,  $H_A$  in  $CH_AH_B$ ), 3.11 (1H, d, J = 18.7 Hz,  $H_{\rm B}$  in CH<sub>A</sub> $H_{\rm B}$ ), 2.77 (1H, brs,  $H_{\rm B}$  in NCH<sub>A</sub> $H_{\rm B}$ ), 2.15 (s, 3H, CH<sub>3</sub> in CH<sub>3</sub>C=N), 1.21 (1H, brs,  $H_B$  in NCH<sub>A</sub>H<sub>B</sub>CH<sub>A</sub>H<sub>B</sub>), 1.11 (1H, brs, CH in CH<sub>2</sub>CH<sub>3</sub>), 0.99 (1H, brs, CH in CH<sub>2</sub>CH<sub>3</sub>), 0.78 (1H, brs,  $H_A$  in NCH<sub>A</sub>H<sub>B</sub>CH<sub>A</sub>H<sub>B</sub>), 0.74 (3H, t, J = 6.7 Hz, CH<sub>3</sub> in CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>):  $\delta$  169.64 (Cq, C=N), 165.90 (Cq, C=O), 142.14 (C<sub>1</sub> in Ar), 128.24 (CH, C<sub>3</sub>+C<sub>5</sub>, Ar), 126.61 (CH, C<sub>4</sub>, Ar), 126.25 (CH, C<sub>2</sub> + C<sub>6</sub>, Ar), 51.21 (NCH<sub>A</sub>H<sub>B</sub>), 46.80 (CH, CH-N), 44.72 (CH<sub>A</sub>H<sub>B</sub>), 26.09 (CH<sub>2</sub> in NCH<sub>A</sub>H<sub>B</sub>CH<sub>A</sub>H<sub>B</sub>), 24.27 (CH<sub>3</sub>C=N), 20.02 (CH<sub>2</sub> in CH<sub>2</sub>CH<sub>3</sub>), 13.63 ( $CH_3$  in  $CH_2CH_3$ ). The complex is soluble in chloroform, dichloromethane, acetonitrile, and methanol.

 $CuL^{H}\cdot 2H_2O$  (2·2H<sub>2</sub>O). Copper(II) acetate monohydrate (42 mg, 0.21 mmol) and H<sub>2</sub>L<sup>H</sup> (110 mg, 0.21 mmol) in DMF (2 mL) were stirred at 80 °C under argon for 2.5 h. The mixture was cooled to room temperature and placed in the refrigerator overnight. The crystals that formed were filtered off, washed with water, and dried in air. Yield: 115 mg, 94% of brownish red crystals. Anal. Calcd for  $C_{30}H_{40}CuN_6O_2\cdot 2H_2O$  ( $M_r$  = 616.25): C, 58.47; H, 7.20; N, 13.64. Found: C, 58.11, 58.34; H, 7.09, 7.21; N, 13.51, 13.57. ESI MS (positive ion mode for <sup>63</sup>Cu isotope): m/z 580 [M + H]<sup>+</sup>, 602 [M + Na]<sup>+</sup>. IR (most characteristic bands, cm<sup>-1</sup>): 3466 br, 3397 br, 2954 m, 2928 m, 2870 m, 1633 s, 1590 vs, 1579 s, 1448 s, 1385 vs, 1335 vs, 1069 s, 765 s, 700 vs, 595 vs, 520 vs. The complex is soluble in methanol, ethanol, chloroform, dichloromethane, and acetonitrile.

 $PdL^{H}\cdot 3H_2O$  (3·3H<sub>2</sub>O). Bis(acetonitrile)palladium(II) chloride (52 mg, 0.2 mmol), H<sub>2</sub>L<sup>H</sup> (104 mg, 0.2 mmol), and sodium acetate trihydrate (26 mg, 0.19 mmol) in DMF (1.5 mL) were stirred at 90 °C for 3 h. The mixture was cooled to room temperature and placed in the refrigerator overnight. The crystals that formed were filtered off, washed with acetonitrile–water 1:1, and dried in air. Yield: 70 mg, 56% of yellowish crystals. Anal. Calcd for C<sub>30</sub>H<sub>40</sub>N<sub>6</sub>O<sub>2</sub>Pd·3H<sub>2</sub>O ( $M_r$  = 677.14): C, 53.21; H, 6.85; N, 12.41. Found: C, 53.42; H, 6.37; N, 12.33%. ESI MS (positive ion mode for <sup>106</sup>Pd isotope): m/z 623 [M +

H]<sup>+</sup>, 645 [M + Na]<sup>+</sup>. IR (most characteristic bands, cm<sup>-1</sup>): 2958 m, 2928 m, 2868 m, 1644 s, 1606 vs, 1494 m, 1381 vs, 1362 vs, 1333 vs, 1067 vs, 751 s, 699 vs, 511 s. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.43 (2H, d, *J* = 7.3 Hz, CH in Ar), 7.28 (2H, t, *J* = 7.0 Hz, CH in Ar), 7.20 (1H, t, *J* = 7.3 Hz, CH in Ar), 5.00 (1H, s, CH–N), 3.93 (1H, brs, *H*<sub>A</sub> in NCH<sub>A</sub>H<sub>B</sub>), 3.30 (1H, d, *J* = 18.3 Hz, *H*<sub>A</sub> in CH<sub>A</sub>H<sub>B</sub>), 3.21 (1H, d, *J* = 17.6 Hz, H<sub>B</sub> in CH<sub>A</sub>H<sub>B</sub>), 3.14–3.02 (1H, m, H<sub>B</sub> in NCH<sub>A</sub>H<sub>B</sub>), 2.14 (3H, s, CH<sub>3</sub> in CH<sub>2</sub>CH<sub>2</sub>), 0.89 (1H, brs, CH in CH<sub>2</sub>CH<sub>2</sub>), 0.74 (3H, t, *J* = 7.1 Hz, CH<sub>3</sub> in CH<sub>2</sub>CH<sub>3</sub>). The complex is soluble in dichloromethane and acetonitrile.

NiL<sup>OMe</sup> (4). NiCl<sub>2</sub>·6H<sub>2</sub>O (48 mg, 0.2 mmol) and H<sub>2</sub>L<sup>OMe</sup> (120 mg, 0.21 mmol) in DMF (2 mL) were stirred at 105 °C for 22 h. The mixture was cooled to room temperature, and the red crystals that formed were filtered off, washed with water, and dried in air. Yield: 112 mg, 88%. Anal. Calcd for C<sub>32</sub>H<sub>44</sub>NiN<sub>6</sub>O<sub>4</sub> (M<sub>r</sub> = 635.42): C, 60.49; H, 6.98; N, 13.93. Found: C, 60.68, 60.80; H, 7.10, 7.31; N, 13.27, 13.40. ESI MS (positive ion mode for <sup>58</sup>Ni isotope): m/z 635  $[M + H]^+$ , 657  $[M + Na]^+$ . IR (most characteristic bands, cm<sup>-1</sup> <sup>1</sup>): 3054 w, 2955 m, 2933 m, 2883 w, 1648 vs, 1616 vs, 1509 s, 1442 m, 1357 s, 1234 vs, 1166 s, 1070 s, 1019 s, 848 vs, 607 s. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.35 (2H, d, J = 7.5 Hz, CH in Ar), 6.85 (2H, d, J = 7.7 Hz, CH in Ar), 4.71 (1H, s, CH-N), 3.79 (1H, brs, H<sub>A</sub> in  $NCH_AH_B$ , 3.77 (3H, s,  $CH_3$  in  $OCH_3$ ), 3.16 (1H, d, J = 19.1 Hz,  $H_A$ in  $CH_AH_B$ ), 3.10 (1H, d, J = 20.5 Hz,  $H_B$  in  $CH_AH_B$ ), 2.79 (1H, t, J = 12.6 Hz, H<sub>B</sub> in NCH<sub>A</sub>H<sub>B</sub>), 2.17 (3H, s, CH<sub>3</sub> in CH<sub>3</sub>C=N), 1.24 (1H, brs, CH in CH<sub>2</sub>CH<sub>2</sub>), 1.14 (1H, brs, CH in CH<sub>2</sub>CH<sub>2</sub>), 1.01 (1H, brs, CH in  $CH_2CH_2$ ), 0.82 (1H, brs, CH in  $CH_2CH_2$ ), 0.75 (3H, t, J = 7.0Hz,  $CH_3$  in  $CH_2CH_3$ ). The complex is soluble in chloroform, dichloromethane, acetonitrile, and methanol.

*CuL*<sup>OMe</sup> (5). Copper(II) acetate monohydrate (40 mg, 0.2 mmol) and  $H_2L^{OMe}$  (118 mg, 0.2 mmol) in DMF (2 mL) were stirred at 85 °C under argon for 3 h. In several minutes the color of the solution changed from blue to green, and after 0.5 h a precipitate appeared. The mixture was cooled to room temperature, and the crystals were filtered off, washed with 50% acetonitrile–50% water (0.5 mL), and dried in air. Yield: 103 mg, 80% of brown crystals. Anal. Calcd for  $C_{32}H_{44}CuN_6O_4$  ( $M_r = 640.28$ ): C, 60.03; H, 6.93; N, 13.13. Found: C, 60.14, 60.10; H, 6.79, 6.75; N, 13.15, 13.07. ESI MS (positive ion mode for <sup>63</sup>Cu isotope): m/z 640 [M + H]<sup>+</sup>, 662 [M + Na]<sup>+</sup>. IR (most characteristic bands, cm<sup>-1</sup>): 3046 m, 2955 m, 293 0m, 2873 w,

2861 w, 1648 vs, 1624 vs, 1579 s, 1509 vs, 1359 s, 1323 vs, 1235 vs, 1020 s, 846 vs, 526 vs. The product is very soluble in chloroform ( $\geq$ 50 mg/mL), has good solubility in methanol ( $\geq$ 13 mg/mL), is moderately soluble in acetonitrile ( $\geq$ 1 mg/mL), and is sparingly soluble in dimethylformamide ( $\leq$ 0.5 mg/mL).  $PdL^{OMe} \cdot 0.5H_2O$  (6.0.5H<sub>2</sub>O). A mixture of bis(acetonitrile)-

palladium(II) chloride (66 mg, 0.25 mmol) and  $H_2 L^{OMe}$  (134 mg, 0.23 mmol) in DMF (1.5 mL) was stirred at 65 °C for 21 h. The volatile components of the reaction mixture were removed under reduced pressure. The residue was washed on a glass microfiber filter with acetonitrile (20 mL) and then with dichloromethane (20 mL). The acetonitrile solution was passed through a silica column by using acetonitrile as eluent. The fraction containing the palladium complex was evaporated, combined with dichloromethane solution, and recrystallized. Yield: 30 mg, 19% of yellow crystals. Anal. Calcd for  $C_{32}H_{44}N_6O_4Pd \cdot 0.5H_2O$  ( $M_r = 692.16$ ): C, 55.53; H, 6.55; N, 12.14. Found: C, 55.57, 55.73; H, 6.53, 6.45; N, 11.99, 11.99. ESI MS (positive ion mode for <sup>106</sup>Pd isotope): m/z 683 [M + H]<sup>+</sup>, 705 [M + Na]<sup>+</sup>. IR (most characteristic bands, cm<sup>-1</sup>): 3055 w, 2954 m, 2932 m, 2879 w, 1651 vs, 1621 vs, 1509 s, 1369 s, 1235 vs, 1055 s, 1020 vs, 846 vs, 603 s. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.34 (2H, d, J = 8.5 Hz, CH in Ar), 6.81 (2H, d, J = 8.6 Hz, CH in Ar), 4.94 (1H, s, CH–N), 3.95 (1H, m, H<sub>A</sub> in NCH<sub>A</sub>H<sub>B</sub>), 3.76 (3H, s, CH<sub>3</sub> in OCH<sub>3</sub>), 3.24 (1H, dd, J = 17.4, 2.5 Hz,  $H_A$  in  $CH_AH_B$ ), 3.16 (1H, dd, J = 17.7, 4.2 Hz,  $H_{\rm B}$  in CH<sub>A</sub> $H_{\rm B}$ ), 3.09 (1H, m,  $H_{\rm B}$  in NCH<sub>A</sub> $H_{\rm B}$ ), 2.14 (3H, s, CH<sub>3</sub> in  $CH_3C=N$ , 1.23 (1H, brs, CH in  $CH_2CH_2$ ), 1.16 (1H, brs, CH in CH<sub>2</sub>CH<sub>2</sub>), 1.08 (1H, brs, CH in CH<sub>2</sub>CH<sub>2</sub>), 0.95 (1H, brs, CH in  $CH_2CH_2$ ), 0.76 (3H, t, J = 7.2 Hz,  $CH_3$  in  $CH_2CH_3$ ). UV-vis (CH<sub>2</sub>Cl<sub>2</sub>),  $\lambda_{max}$ , nm ( $\epsilon$ , M<sup>-1</sup> cm<sup>-1</sup>): 502 (5250), 463 (5073), 390 (3177), 323(11730). The complex is soluble in dichloromethane and acetonitrile.

Crystallographic Structure Determination. X-ray diffraction quality single crystals of 2.2EtOH were grown from ethanol, 4 and 5 were obtained by slow evaporation of chloroform-ethanolic solutions, and 6 was obtained from dichloromethane. The measurements were performed on Gemini (H<sub>2</sub>L<sup>OMe</sup>), Bruker D8 Venture (2. 2EtOH and 6), and Bruker X8 APEXII CCD (4 and 5) diffractometers. Single crystals were positioned at 55, 30, 27, 30, and 24 mm from the detector, and 4222, 1122, 641, 1122, and 444 frames were measured, each for 3/12, 3, 24, 30, and 10 s over 1, 1, 0.5, 0.5 and 0.5° scan width for  $H_2L^{OMe}$ , 2·2EtOH, and 4–6, respectively. The data were processed using SAINT and STOE X-RED software.<sup>38,39</sup> Crystal data, data collection parameters, and structure refinement details are given in Table 1. The structures were solved by direct methods and refined by full-matrix least-squares techniques. Non-H atoms were refined with anisotropic displacement parameters. H atoms were inserted in calculated positions and refined with a riding model. The following computer programs and hardware were used: structure solution, SHELXS-2014; structure refinement, SHELXL-2014;<sup>40</sup> molecular diagrams, ORTEP;<sup>41</sup> computer, Intel CoreDuo. CCDC file numbers 1996061  $(H_2L^{OMe})$ , 1996062 (5), 1996063 (4), 2005715 (2·EtOH), and 1996065 (6).

Electrochemistry and Spectroelectrochemistry. Cyclic voltammograms of 0.5 mM DCM and ACN solutions of 1-6 containing 0.1 M nBu<sub>4</sub>NPF<sub>6</sub> supporting electrolyte were measured in a homemade miniature electrochemical cell using a platinum-disk or glassy-carbon-disk working electrode (from Ionode, Australia), a platinum wire as the counter electrode, and silver wire as a pseudo reference electrode. Ferrocene served as the internal potential standard, and the potentials were determined vs the ferricenium/ ferrocene couple. A Heka PG310USB (Lambrecht, Germany) potentiostat with a PotMaster 2.73 software package was used in cyclic voltammetric and spectroelectrochemical studies. In situ spectroelectrochemical measurements were performed under an argon atmosphere in a spectroelectrochemical cell kit (AKSTCKIT3) with a Pt microstructured honeycomb working electrode, purchased from Pine Research Instrumentation. UV-vis-NIR measurements of chemically oxidized compounds were performed in an oxygen-free glovebox using quartz cells of 1.0 cm path length from Agilent Technologies. Nitrosonium tetrafluoroborate (NOBF<sub>4</sub>, 98%) as an oxidizing agent purchased from Alfa Aesar was used as received. An Avantes Model AvaSpec-2048x14-USB2 spectrometer served for recording UV-vis-NIR spectra in both spectroscopic and spectroelectrochemical studies. Halogen and deuterium lamps were used as light sources (Avantes, Model AvaLight-DH-S-BAL). The cell was positioned in a CUV-UV Cuvette Holder (Ocean Optics) connected to the diode-array UV-vis-NIR spectrometer by optical fibers. UV-vis-NIR spectra were processed using the AvaSoft 7.7 software package. EPR spectra were recorded with an EMXplus X-band EPR spectrometer (Bruker, Germany).

**Computational Details.** Standard B3LYP/6-311+ $G^{*42-47}$  geometry optimization of neutral <sup>1</sup>[NiL<sup>H</sup>]<sup>0</sup> in the singlet spin state and <sup>m</sup>[ML<sup>OMe</sup>]<sup>4</sup>, M = Ni, Cu, in various charge q and spin states (with spin multiplicity m) was performed using the Gaussian16<sup>48</sup> program package. The unrestricted DFT formalism has been used for all complexes. Solvent effects in dichloromethane were approximated by the solvation model based on density (SMD) modification<sup>49</sup> of the integral equation formalism polarizable continuum model as implemented in Gaussian16. The stability of the optimized structures was confirmed by vibrational analysis (no imaginary vibrations). Excited-state energies with corresponding electron transitions were evaluated using the time-dependent DFT method<sup>50–52</sup> for 70 states. The MOLEKEL package<sup>53</sup> has been used for the visualization of molecular orbitals and spin densities. The atomic charges and d electron populations on the central metal atom have been obtained via the natural population analysis (NPA)<sup>54–56</sup> as implemented in Gaussian16.

**Catalytic Studies.** The microwave-assisted peroxidative oxidation of neat styrene was performed in a focused Anton Paar Monowave 300 reactor, using a 10 mL capacity Pyrex tube with a 13 mm internal diameter and equipped with a rotational system and an IR temperature detector. Styrene (1.0 mmol), complex 2 or 5 (5 mmol), 30 wt % aqueous  $H_2O_2$  (4 mmol), and chlorobenzene as an internal standard (100  $\mu$ L) were placed in the tube, and the tube was sealed. The reaction mixture was MW-irradiated with stirring at 80 °C for 15–60 min. To follow the reaction evolution, 100  $\mu$ L aliquots were withdrawn at the desired reaction times and, after they were cooled, the samples were centrifuged (to remove the catalyst, which is insoluble in the reaction media at room temperature) and analyzed by gas chromatography (GC).

GC measurements were carried out using a Perkin–Elmer Clarus 600 C with an FID detector and a capillary column (DB-WAX, column length 30 m, internal diameter 0.32 mm) and the Jasco-Borwin v.1.50 software. The temperature of the injector was 200 °C. The initial temperature was maintained at 90 °C for 2 min, then raised up to 150 °C (10 °C/min), and then directly up to 250 °C (50 °C/min) and finally kept at this temperature for 8 min. Helium was used as the carrier gas. The products were identified by comparison of their retention times with known reference compounds, and the styrene conversion values (result of two concordant assays) were determined by the internal standard method.

The catalyst reusability in consecutive runs was tested by separating the used catalyst from the reaction mixture by centrifugation followed by filtration of the supernatant solution, washing with acetonitrile/ water, and drying in air. The new run was initiated by addition of the fresh reagents (see above) in addition to the used catalyst. After completion of each run, the products were analyzed by GC as described above.

For the nitroaldol C–C couplings an OS1025 STEM Omni (Electrothermal) reactor was used. In a Teflon-capped 10 × 25 mL Pyrex tube were placed benzaldehyde (1.0 mmol), nitroethane (4.0 mmol), **1**, **3**, **4** or **6** (5.0  $\mu$ mol, 0.5 mol % vs. benzaldehyde), and the chosen solvent (2.0 mL). The reaction mixture was stirred (600 rpm) under ambient conditions up to 48 h. At the desired time, the reaction was stopped and the reaction mixture centrifuged to remove the solids. Subsequent evaporation of the solvent yielded the crude product. When water was used as the solvent, the mixture was dried under vacuum. A sample was dissolved in DMSO-*d*<sub>6</sub> and analyzed at room temperature by <sup>1</sup>H (300 MHz) NMR on a Bruker Avance II+ 300 (UltraShieldMagnet) spectrometer using tetramethylsilane (Si-

 $(CH_3)_4)$  as an internal reference. The yield of the  $\beta$ -nitroethanol products (relative to benzaldehyde) was established using 1,2-dimethoxyethane as an internal standard. The values of the vicinal coupling constants between the  $\alpha$ -N–C–H and  $\alpha$ -O–C–H protons (J = 7-9 and 3.2–4 Hz, respectively) helped in the identification of the syn or anti isomer.

For the catalyst recycling experiments, the used catalyst was separated, washed with several portions of water, and dried in an oven at 60  $^{\circ}$ C. Each cycle was initiated after the preceding one upon addition of new typical portions of all other reagents (see above). After completion of each run, the products were analyzed by NMR as described above.

The ambient ultrasound (US) assisted Knoevenagel reactions were carried out in an Elma Transsonic 600/H ultrasonic bath. In a capped round-bottom Pyrex flask were placed benzaldehyde (1.0 mmol), malononitrile (2.0 mmol), **1**, **3**, **4** or **6** (10.0  $\mu$ mol, 1 mol % vs. benzaldehyde), and acetonitrile (2 mL) under ambient conditions. The flask was immersed in the ultrasonic bath in an open atmosphere for up to 3 h. Then, the reaction mixture was centrifuged and the solids were removed by filtration. The filtrate was evaporated, and the residue was dissolved in CDCl<sub>3</sub> and analyzed by <sup>1</sup>H NMR (see above).

Blank experiments, in the absence of **1–6**, were performed for all (oxidation, and Henry and Knoevenagel C–C couplings) reaction types under the optimized conditions, and no significant reagent conversion was detected (e.g., 2% for the  $\beta$ -nitroethanol products). Moreover, experiments with the respective precursor salts (NiCl<sub>2</sub>· 6H<sub>2</sub>O, Cu(OAc)<sub>2</sub>·H<sub>2</sub>O, and [PdCl<sub>2</sub>(NCMe)<sub>2</sub>]), also run using the optimized conditions, led to yields much lower than those found for **1–6**.

#### RESULTS AND DISCUSSION

Synthesis of Hexaaza Macrocyclic Proligands. The macrocyclic compounds trans-IX (Scheme 1) were prepared in several steps as reported previously.<sup>32-35</sup> In contrast to thiosemicarbazide, which exists in solution in the two tautomeric forms thione and thiol, the one-ol tautomerism is not typical for semicarbazide and macrocycles IX (Ar = Ph, 4-MeOC<sub>6</sub> $H_4$ ) in Scheme 1. The alkylation of the latter does not lead to alkylation of the chalcogen in the semicarbazide (or semicarbazone) fragment as occurs in the case of thio(seleno)semicarbazides or thio(seleno)semicarbazones. Instead, a selective butylation of hydrazinic nitrogen atoms occurred in the presence of NaH in DMF with the generation of  $H_{2}L^{H}$  and  $H_2L^{OMe}$  (see Chart 3). The formation of these products was confirmed by 1D (<sup>1</sup>H, <sup>13</sup>C) and 2D (<sup>1</sup>H-<sup>1</sup>H COSY, <sup>1</sup>H-<sup>1</sup>H TOCSY, <sup>1</sup>H-<sup>1</sup>H NOESY, <sup>1</sup>H-<sup>13</sup>C HSQC, <sup>1</sup>H-<sup>13</sup>C HMBC) NMR spectra, ESI mass spectrometry, and single-crystal X-ray diffraction of  $H_2L^{OMe}$  (vide infra).

Synthesis of Complexes. Complexes 1 and 4 were prepared by reactions of NiCl<sub>2</sub>· $6H_2O$  with  $H_2L^H$  and  $H_2L^{OMe}$ in a 1:1 molar ratio upon heating in DMF in 88 and 83% yields, respectively. Compounds 2.2H2O and 5 were synthesized similarly starting from Cu(OAc)<sub>2</sub>·H<sub>2</sub>O in 94 and 80% yields, respectively. The reaction of  $PdCl_2(CH_3CN)_2$  with H<sub>2</sub>L<sup>H</sup> and NaOAc as a base in a 1:1:1 molar ratio in DMF afforded 3.3H<sub>2</sub>O in 56% yield, while that of PdCl<sub>2</sub>(CH<sub>3</sub>CN)<sub>2</sub> with  $H_2 L^{OMe}$  in a 1:1 molar ratio in DMF led to crude 6, which was purified by column chromatography on silica to give pure 6.0.5H<sub>2</sub>O in 19% yield. All six complexes in ESI mass spectra measured in positive ion mode gave strong peaks attributed to  $[M + H]^+$  and  $[M + Na]^+$  ions (see Figures S12–S14). <sup>1</sup>H NMR spectra were in accordance with  $C_i$  molecular symmetry for 1, 3, 4, and 6. The formation of nickel(II), copper(II), and palladium(II) complexes with  $H_2L^H$  and  $H_2L^{OMe}$  was further confirmed by single-crystal X-ray diffraction studies.

**X-ray Crystallography.** The results of X-ray diffraction studies of 2·EtOH,  $H_2L^{OMe}$ , and 4–6 are shown in Figures 1–3, respectively, with selected bond distances and bond



**Figure 1.** ORTEP plot of **CuL**<sup>H</sup>**·2EtOH** (**2·2EtOH**) with the atomlabeling scheme and thermal ellipsoids drawn at the 50% probability level. The cocrystallized solvent is not shown. Selected bond distances (Å) and bond angles and dihedral angles (deg): Cu–N1 = 1.9671(17), Cu–N3 = 1.8699(17) Å; N1–Cu–N3 = 82.69(7), N1<sup>i</sup>–Cu–N3 = 97.31(7),  $\theta_{N3-C1-C2-C3} = -55.4(2)$ ,  $\theta_{C1-C2-C3-N1^i} =$ 21.9(3) (i denotes an equivalent atom generated by the symmetry transformation -x + 1, -y + 1, -z + 1).

angles quoted in the legends. All compounds crystallized as racemates: the copper(II) complex **2·EtOH** in the triclinic centrosymmetric space group  $P\overline{1}$ , **5** in the monoclinic space group  $P2_1/c$ , and  $H_2L^{OMe}$ , **4**, and **6** in the orthorhombic space group *Pbca*. The nickel(II), copper(II), and palladium(II) in **2** and **4**–**6** adopt a square-planar coordination geometry. The structures of  $H_2L^{OMe}$ , **2·EtOH**, and **4**–**6** are centrosymmetric. In  $H_2L^{OMe}$  the inversion center is in the middle of the macrocycle, while in **2·EtOH** and **4**–**6** the central metal ions lie on the inversion center. The conformation adopted by the free ligand  $H_2L^{OMe}$  does not change markedly upon complex formation, as shown for example for NiL<sup>OMe</sup> in Figure 2.

The Ni–N1 bond distance is significantly (by ca. 0.025 Å) longer than Ni-N3 in nickel(II) complex 4. The difference between these two bonds in the nickel(II) complex with IX where Ar = Ph (Scheme 1) with Ni $-N_{hydrazine} = 1.900(11)$  Å and Ni $-N_{amide} = 1.860(11)$  Å is not significant.<sup>57</sup> In the case of copper(II) complexes 2·EtOH and 5 the bond length difference is quite significant and amounts to ca. 0.1 Å, while the difference in Pd-N<sub>hvdrazine</sub> and Pd-N<sub>amide</sub> interatomic distances has vanished in 6 (statitically equal within  $3\sigma$ ). This is not the case for palladium complexes with tridentate semicarbazonates, i.e. 2.014(3) and 1.966(3) Å in the dipalladium complex with the trianion of 2-hydroxy-3methoxybenzaldehyde semicarbazone  $Pd_2(L)Cl(PPh_3)_3^{58}$  or 2.033(3) and 1.976(3) Å in Pd(HL)PPh<sub>3</sub>, where  $H_3L = 2$ hydroxyacetophenone semicarbazone.<sup>59</sup> The trend M-N1 > M-N3 is typical for first-row transition-metal complexes with isothiosemicarbazides, where the electronically distinct termi-



**Figure 2.** (a) ORTEP plot of  $H_2L^{OMe}$  with the atom-labeling scheme and thermal ellipsoids drawn at the 20% probability level. Selected bond distances (Å) and selected torsion angles (deg): N1–N2 = 1.424(3), N2–C4 = 1.400(3), C4–N3 = 1.337(3), C4–O1 = 1.218(3), N3–C1 = 1.448(3), C1–C2 = 1.534(4), C2–C3 = 1.508(4) Å;  $\theta_{N3-C1-C2-C3} = -59.3(3)$ ,  $\theta_{C1-C2-C3-N1}^{i} = 21.0(3)$  (i denotes an equivalent atom generated by the symmetry transformation -x + 1, -y + 1, -z + 1). (b) ORTEP plot of NiL<sup>OMe</sup> (4) with the atom-labeling scheme and thermal ellipsoids drawn at the 50% probability level. Selected bond distances (Å) and bond angles and torsion anlgles (deg): Ni–N1 = 1.8570(18), Ni–N3 = 1.8329(16); N1–Ni–N3<sup>1</sup> = 96.52(7) (i denotes an equivalent atom generated by the symmetry transformation -x, -y, -z + 1), N1–Ni– N3 = 83.48(7),  $\theta_{N3-C1-C2-C3} = -58.9(2)$ ,  $\theta_{C1-C2-C3-N1^i} = 27.9(3)$ .

nal amine groups produce a somewhat different anisotropic ligand field.  $^{\rm 27}$ 

Upon coordination of the macrocyclic ligands to metals two almost flat five-membered chelate rings and two six-membered rings with a puckered or envelope conformation are formed. The deviations of atom C1 from the mean plane through M, N3 (N3<sup>i</sup>), C2, C3 and N1<sup>i</sup> (N1) are summarized in Table S1 in the Supporting Information.

A comparison of torsion angles quoted in the legends to Figures 2 and 3 for  $H_2L^{OMe}$ ,  $NiL^{OMe}$ ,  $CuL^{OMe}$ , and  $PdL^{OMe}$  shows that insertion of palladium(II) into the macrocycle causes its largest conformational change. This was expected, since it is known that 4d metals have ionic radii about 0.1–0.2 Å greater than those of 3d metals.<sup>60</sup>

Another feature of note is the lack of proton donors in the molecules of the metal complexes, which makes intermolecular interactions via hydrogen bond formation impossible. There are only van der Waals interactions between the molecules of **2** and **4**–**6**. In contrast, the nickel(II) complex of *trans*-**IX** (Ar = Ph) is involved in strong intermolecular interactions of lactam groups via centrosymmetric N–H…O hydrogen bonds, as shown in Figure S15.<sup>57</sup> As mentioned previously, this might be a reason for the low solubility of the nickel(II) complexes in common organic solvents and water.

As 3d metal complexes with isothiosemicarbazide- and (iso)thiocarbazide-based ligands (open chain and macrocyclic) revealed noninnocent behavior,<sup>61,27</sup> it was of particular interest



**Figure 3.** (a) ORTEP plot of **CuL**<sup>OMe</sup> (5) with the atom-labeling scheme and thermal ellipsoids drawn at the 50% probability level. Selected bond distances (Å) and bond angles and torsion angles (deg): Cu–N1 = 1.9623(18), Cu–N3 = 1.8666(17); N1–Cu–N3<sup>i</sup> = 97.17(7) (i denotes an equivalent atom generated by the symmetry transformation -x, -y + 1, -z), N1–Cu–N3 = 82.83(7),  $\theta_{N3-C1-C2-C3} = -59.4(2)$ ,  $\theta_{C1-C2-C3-N1^i} = 26.4(3)$ . (b) ORTEP plot of **PdL**<sup>OMe</sup> (6) with the atom-labeling scheme and thermal ellipsoids drawn at the 50% probability level. Selected bond distances (Å) and bond angles and torsion angles (deg): Pd–N1 = 1.9624(15), Pd–N3 = 1.9545(15); N3<sup>i</sup>–Pd–N1 = 98.65(6) (i denotes an equivalent atom generated by the symmetry transformation -x, -y, -z + 1), N1–Pd–N3 = 81.35(6),  $\theta_{N3-C1-C2-C3} = -64.6(2)$ ,  $\theta_{C1-C2-C3-N1} = 42.5(2)$ .

to study the spectroelectrochemical properties of 1-6 and identify, if possible, the site of electron transfer by performing, in addition, DFT calculations.

Electrochemistry and Spectroelectrochemistry. The redox properties of 1-6 were investigated by cyclic voltammetry in dichloromethane (DCM) or in acetonitrile (ACN) containing tetrabutylammonium hexafluorophosphate as the supporting electrolyte. One oxidation wave was observed for all investigated complexes 1-6 in DCM in the potential window available, as shown in cyclic voltammograms in Figure 4. Nickel(II) complexes exhibit both electrochemical and chemical reversibility upon anodic oxidation at 100 mV s<sup>-1</sup> with the half-wave potentials  $E_{1/2}$  = +0.60 and +0.57 V vs Fc<sup>+</sup>/ Fc for 1 and 4, respectively. The redox waves for copper(II) complexes 2 and 5 are quasi-reversible and with the lowest redox potentials of the oxidative response with  $E_{pa} = +0.45$  and +0.42 V vs  $Fc^+/Fc$ , respectively. In addition, a small new counterpeak is observed upon a backward scan, indicating the lower stability of the oxidized state for copper(II) complexes in comparison to the nickel(II) analogues. Note that complexes 4-6 with R = OMe show slightly lower redox potentials of the aforementioned oxidation processes. In contrast to nickel(II) and copper(II) complexes, the palladium(II) complexes 3 and 6 reveal a fully irreversible oxidation peak with much higher redox potentials of the oxidative response at +0.83 and +0.82 Vvs Fc<sup>+</sup>/Fc, respectively. Similar redox behavior was observed in acetonitrile solutions at a GC working electrode with  $E_{1/2}$  =



**Figure 4.** Cyclic voltammograms of 1-6 in the region of the first anodic peak (1, dark cyan trace; 2, red trace; 3, dark yellow trace; 4, blue trace; 5, black trace; 6, magenta trace), all in 0.1 M  $nBu_4NPF_6/DCM$  at a Pt working electrode (scan rate 100 mV s<sup>-1</sup>).

+0.57 V for 1,  $E_{1/2}$  = +0.56 V for 4,  $E_{pa}$  = +0.38 V for 2,  $E_{pa}$  = +0.36 V for 5,  $E_{pa}$  = +0.81 V for 3, and  $E_{pa}$  = +0.79 V for 6 (all vs Fc<sup>+</sup>/Fc).

Upon *in situ* anodic oxidation of 1 in a spectroelectrochemical cell with a Pt microstructured honeycomb working electrode, a nearly reversible redox couple in the corresponding cyclic voltammogram at 10 mV s<sup>-1</sup> in *n*Bu<sub>4</sub>NPF<sub>6</sub>/DCM was observed (see inset in Figure 5a) with a simultaneous evolution of new absorption bands with maxima at 324, 427, 724, and 874 nm (Figure 5a). At the same time, an isotropic Xband EPR spectrum was observed with a high g value of 2.1004 and the line width  $\Delta H_{pp} = 28.5$  G at room temperature, indicating a strong noninnocent behavior of the ligand (see inset in Figure 5b). The same UV–vis–NIR and EPR spectroelectrochemical responses were found for the nickel(II) analogue 4 (Figure S16), confirming the very small influence of the OCH<sub>3</sub> group of the ligand on the redox behavior of the investigated complexes.

To investigate the possibility of tautomerism between nickel(III)-ligand and nickel(II)-ligand radical states for our oxidized 1, we performed an *ex situ* EPR spectroelectrochemical experiment, in which 1 was electrolyzed in 0.1 M  $nBu_4NPF_6/DCM$  at the first anodic peak. After bulk electrolysis an EPR tube with the sample under argon was immediately immersed into liquid nitrogen, and EPR spectra were recorded. Figure 6a shows the EPR spectrum of the one-electron-oxidized 1 at 100 K (black trace).

Two anisotropic EPR signals with different *g* values are clearly seen, in contrast to the single isotropic EPR signal (S = 1/2) measured at 298 K. In the latter case the *g* value of 2.1004 is between those for nickel(III)–ligand and nickel(II)–ligand radical species, indicating the formation of a ligand radical with a marked delocalization of the unpaired spin onto orbitals of the nickel ion. Simulation of this EPR signal (see blue trace in Figure 6a) yielded g = 2.215(0), 2.079(8), 2.055(3). An additional EPR signal emerged at low temperatures (see red trace in Figure 6a), whose intensity increased by a decrease in the temperature, gave g = 2.269(8), 2.246(7), 2.020(5), which can be attributed to Ni(III) species. The *g* matrix deduced for the Ni(III) species is characteristic of a low-spin 3d<sup>7</sup> electronic configuration with a  $(d_{xy}d_{yz})^6d_z^{21}$  ground state.<sup>62</sup> The



**Figure 5.** In situ spectroelectrochemistry of 1 in 0.1 M  $nBu_4NPF_6/DCM$  at 10 mV s<sup>-1</sup>. (a) UV–vis–NIR spectra detected simultaneously upon the *in situ* oxidation in the region of the first anodic voltammetric peak (blue lines). Inset: the corresponding cyclic voltammogram. (b) 3D view of the potential dependence of UV–vis–NIR spectra measured during a cyclic voltammetric scan. Inset: EPR spectrum registered in the region of the first anodic wave at 298 K. The color-highlighted potential regions in the voltammogram shown in (a) correspond to the color-highlighted optical spectra depicted in (b).

intensities of the simulated EPR spectra, which fit the experimental EPR spectrum at 100 K well (see dark cyan trace in Figure 6a), determined by double integration, indicate that the ratio of the Ni(III) species to the Ni(II)–ligand radical species is 0.3:1 at 100 K.

As expected, less reversible or irreversible spectroelectrochemical response was observed for copper(II) and palladium-(II) complexes, as illustrated in Figure S17. Upon oxidation of 5 at a 5 mV s<sup>-1</sup> scan rate the voltammogram was nearly irreversible (Figure S17a) and a new absorption band at 370 nm arose (Figure S17c). This band only partially disappeared after a backward scan, confirming irreversible changes upon oxidation. In the case of 2 the band appeared at 358 nm (not shown). Even more irreversible behavior was found for palladium(II) complexes 3 and 6, as seen in Figure S17b,d. Chemical oxidation of 0.5 mM solutions of complexes 4 and 5 in DCM with a stoichiometric amount of NOBF<sub>4</sub> ( $E^{\circ}_{1/2} = 1.00$ V vs Fc<sup>+</sup>/Fc)<sup>63</sup> cleanly afforded one-electron-oxidized products with characteristic UV-vis-NIR spectra (Figure S18).

In the cathodic part the reduction processes are characteristic only for copper(II) complexes **2** and **5**. The best electrochemical reversibility was observed when a GC working electrode was used (Figure S19). A reversible voltammetric response with  $E_{1/2} = -1.63$  V vs Fc<sup>+</sup>/Fc was registered for both



Figure 6. (a) X-band EPR spectrum of oxidized 1 (black trace) simulated as described in the text (the same response was observed for 4, not shown). Experimental EPR parameters: X-band, frequency 9.448 GHz, center field 3130 G, sweep width 1000 G, modulation amplitude 2 G, modulation frequency 100 kHz, time constant 10.24 ms, receiver gain  $1 \times 10^5$ , temperature 100 K. (b) Spin density distribution calculated for the paramagnetic monocharged species  $[4]^+$ .

complexes. Upon *in situ* cathodic reduction of 5 (Figure 7) the reversible redox couple in the corresponding cyclic voltammogram at 10 mV s<sup>-1</sup> in 0.1 M nBu<sub>4</sub>NPF<sub>6</sub>/ACN (inset in Figure 7a) was accompanied by simultaneous evolution of a broad absorption band with a maximum at 420 nm (Figure 7b). A strong decrease in the initial copper(II)  $(d^9, S = 1/2)$  EPR signal (Figure S20) was observed in the analogous spectroelectrochemical experiment directly in the EPR cavity using a large platinum working electrode (see inset in Figure 7b), indicating the reduction of Cu(II) with the formation of a diamagnetic d<sup>10</sup> EPR-silent Cu(I) species. Additionally, upon a voltammetric reverse scan, reoxidation and a nearly full recovery of the initial optical bands were observed, attesting to the chemical reversibility of the cathodic reduction (Figure 7a). As expected, a very similar spectroelectrochemical response was also found for 2 (Figure S21).

**Theoretical Studies.** To get a deeper insight into the electronic structures of 1-6, the geometries of  ${}^{1}[\text{NiL}^{\text{H}}]^{0}$  and  $[\text{ML}^{\text{OMe}}]^{q}$ , q = 0, +1, -1, were optimized by starting from the available X-ray crystallographic data. The structural parameters of the DFT-optimized structures match reasonably well with the experimental metrical parameters from single-crystal X-ray diffraction data, as shown in Table S1. Unlike centrosymmetric  $[\text{NiL}^{\text{OMe}}]^{q}$  complexes, their oxidized copper analogues (q = +1) undergo a symmetry decrease due to a pseudo-Jahn–Teller effect. From the obtained energetics of the optimized geometries (Table S2), DFT calculations indicate that a neutral-spin singlet for  $[\text{NiL}^{\text{OMe}}]^{0}$  is more stable than its triplet



**Figure 7.** In situ spectroelectrochemistry of **5** in 0.1 M  $nBu_4NPF_6/ACN$  at 10 mV s<sup>-1</sup>. (a) 3D view of the potential dependence of UV–vis–NIR spectra measured upon a cyclic voltammetric scan. Inset: the corresponding cyclic voltammogram. (b) UV–vis–NIR spectra detected simultaneously upon the *in situ* reduction in the region of the first cathodic voltammetric peak (red lines). Inset: EPR spectra registered in the region of the first cathodic wave at 298 K.

spin state, and the same holds for [CuL<sup>OMe</sup>]<sup>+</sup>. In Figure 8a, experimental electronic absorption spectra for the nickel(II) complex 4 (black trace in Figure 8a) and those for [4]<sup>+</sup> (red trace), generated electrochemically, are compared with theoretical TD-DFT electronic transitions calculated for 4 in a singlet state (blue columns in Figure 8a) and [4]<sup>+</sup> in a doublet spin state (pink columns). Theoretical calculations using CH<sub>2</sub>Cl<sub>2</sub> solvent effects within the solvation model based on density (SMD) predict very well the experimental transitions found for 4 as well as the existence of three lowenergy transitions observed for  $[4]^+$ . For 4, the first transition at 360 nm with a significant oscillator strength corresponds mainly to that from HOMO to LUMO+1. The shape of the HOMO orbital indicates the strong noninnocent character of the ligand and also the ligand-centered site for oxidation. Indeed, the calculated spin density distribution for paramagnetic monocharged  $[1]^+$  and  $[4]^+$  is similar to the HOMO shape and is located on the central nickel atom and two neighboring nitrogens (see Figure 6b). In the case of  ${}^{2}[4]^{+}$ , the lowest energy intense electron transitions at 878 and 698 nm (see pink columns in Figure 8a) correlate very well with the experimentally observed optical bands. These transitions are attributed to the  $\beta$ -HOMO to  $\beta$ -LUMO transitions ( $\beta$ -HOMO-6 (-0.2735 au)  $\rightarrow \beta$ -LUMO (-0.1726 au) for 698



**Figure 8.** (a) Comparison of the experimental absorption spectra for neutral (black trace) and one-electron-oxidized (red trace) nickel(II) complex 4 and calculated electronic transitions for  ${}^{1}$ [4]<sup>0</sup> (blue columns) and  ${}^{2}$ [4]<sup>+</sup> (pink columns). Inset: B3LYP orbitals contributing to the TD-B3LYP electron transition for  ${}^{2}$ [4]<sup>+</sup> at 878 nm. (b) B3LYP orbitals contributing to the lowest TD-B3LYP electron transition for  ${}^{1}$ [4]<sup>0</sup>.

nm and  $\beta$ -HOMO-2 (-0.2610 au)  $\rightarrow \beta$ -LUMO (-0.1726 au) for 878 nm, with dominating charge transfer from the ligand to the central atom (see the inset in Figure 8a). The relatively small changes in the charge, d electron population, and spin density at the Ni and Cu central atoms (see Table S3) during the redox processes are in full agreement with the noninnocent character of the ligand as well. For <sup>2</sup>[**5**]<sup>0</sup> the spin density is located on the copper and four neigboring nitrogen atoms (see the inset in Figure S22a). Although the calculated optical transitions for <sup>2</sup>[**5**]<sup>0</sup> match the experimental UV-vis bands very well (Figure S22), this is not the case for transitions computed for the charged states (Figure S22).

The documented redox behavior of metal complexes justified further investigation of 1-6 in catalytic oxidation and C-C coupling reactions.

Catalytic Studies. In the present study, the oxidation of styrene to benzaldehyde and C–C coupling reactions at benzaldehyde were chosen as benchmark reactions, on account of their industrial importance.  $^{64-67}$  Metal(II) complexes 1–6 were tested, according to their features, as catalysts for the above reactions under environmentally benign operation conditions: (i) microwave-assisted oxidation of neat styrene to benzaldehyde, (ii) room-temperature Henry C-C coupling of benzaldehyde with nitroethane, and (iii) ultrasound-assisted Knoevenagel condensation of benzaldehyde and malononitrile (Scheme 2). When heating was required (oxidation of styrene), the alternative microwave (MW) energy source was chosen, as it is known<sup>68,69</sup> that MW irradiation improves the yield and selectivity of a process relative to those achieved through conductive heating (where heat from an external source first passes through the walls of the vessel to reach the reaction mixture). Moreover, this efficient method of transferring energy (based on dipole rotation and/or ionic conduction) from the microwaves to the substances being





<sup>a</sup>Abbreviations: MW, microwave; US, ultrasound.

heated leads to increased reaction rates, and therefore, the desired transformations occur in a shorter period of time.

Compounds 2 and 5 selectively catalyze the microwaveassisted oxidation of neat styrene to benzaldehyde using hydrogen peroxide (30% aqueous solution) as the oxidizing agent, under low MW irradiation (25 W) and in the absence of any added solvent (Scheme 2). The reaction conditions were optimized relative to several reaction parameters: namely, MW irradiation power, time, temperature, and catalyst and oxidant amounts. Under the optimized conditions (40 min of irradiation at 80 °C), the catalytic systems afforded benzaldehyde in up to 88 and 81% yields (TOF, turnover frequency, up to  $2.6 \times 10^3$  and  $2.4 \times 10^3$  h<sup>-1</sup>), respectively, for 2 and 5 as the only product (Figure 9).



Figure 9. Benzaldehyde conversion and selectivity obtained from the MW-assisted oxidation of neat styrene, catalyzed by 2 or 5.

The selectivity exhibited by catalysts 2 and 5 is remarkable. In fact, several homo- and heterogeneous Cu(II) catalytic systems previously used  $^{70-73}$  for the oxidation of styrene were not able to afford selective benzaldehyde formation. Among them are copper(II) complexes of a Schiff base derived from salicylaldehyde and *o*-aminobenzyl alcohol,<sup>70</sup> which, encapsulated in zeolite-Y, catalyze the oxidation of styrene by  $H_2O_2$ and, under the optimized reaction conditions, gave five reaction products (styrene oxide, benzaldehyde, 1-phenylethane-1,2-diol, benzoic acid, and phenylacetaldehyde). Other examples are copper(II) complexes with salen ligands tethered onto amino-functionalized graphene oxide<sup>71</sup> (which require acetonitrile as solvent and the sacrificial coreductant isobutyraldehyde) or polymer-anchored copper(II)<sup>72</sup> that led to styrene epoxide, benzaldehyde, and styrene oxide (84% maximum selectivity for benzaldehyde). Recently, types of Cu(II) complexes bearing tris(pyrazolyl)methane C-homoscorpionate ligands immobilized on sucrose derived hydrochars<sup>73</sup> were reported to selectively catalyze the conversion of styrene to benzaldehyde in a homogeneous medium, where the complex immobilization resulted in a decrease in the conversion and selectivity toward benzaldehyde, relative to the values achieved in homogeneous assays.

Even though the metal-catalyzed oxidation of alkenes with hydrogen peroxide has been intensily studied, there is currently no firm opinion on the mechanisms of these reactions.<sup>74</sup> We propose that the MW-assisted oxidation of neat styrene catalyzed by the copper(II) complex 2 or 5 proceeds through a free radical mechanism, where the availability of reversibly reducible copper(II) complexes with bis-semicarbazide hexaaza macrocycles (see Figure 7) by the hydroperoxide is crucial for the oxidation to occur.<sup>36</sup> It could be initiated by the Cuassisted formation of the oxygen-centered radicals hydroxyl and hydroperoxyl, similar to the Fenton chemistry.<sup>75</sup> The sequential addition of these radicals to the styrene double bond gives the 1,2-hydroxyhydroperoxide PhCH(OH)CH<sub>2</sub>OOH as a key intermediate. Further radical-induced fragmentation of the latter leads to the formation of benzaldehyde. In addition, complexes 2 and 5 are much more active than their precursor salt, copper(II) acetate monohydrate, which led to a benzaldehyde maximum yield of 23%. This suggests a favorable role of the macrocyclic ligand in this catalytic oxidation reaction. Moreover, after the removal of catalyst 2 or 5 from the reaction mixture (see the Experimental Section), the reaction did not proceed toward a higher yield of the product of the oxidation of styrene in solution, in accord with the absence of a catalytically active species.

Although the selectivity toward benzaldehyde was maintained at least for three consecutive cycles of the recycling tests (see the Experimental Section), the styrene conversion progressively decreased (46, 32, and 21%, respectively). Therefore, an optimization of the catalytic system is still required.

Compounds 1, 3, 4, and 6 were found to be catalysts for both C–C cross-couplings (Scheme 2). The complexes were tested for the Henry C–C coupling of benzaldehyde with nitroethane, at room temperature, leading to a *syn*- and *anti-β*nitroethanol mixture. The reaction conditions were optimized relative to several parameters (e.g., reaction time, reagent ratios, type and amount of solvent, and amount of catalyst) in order to promote the  $\beta$ -nitroethanol *syn:anti* diastereoselectivity. The optimized catalytic conditions were found to be benzaldehyde (1 mmol), nitroethane (4 mmol), 1 or 4 (5  $\mu$ mol, 0.5 mol % vs benzaldehyde), MeOH (2 mL), and stirring (600 rpm) in air at room temperature for 48 h (Figure 10).

Under the above conditions, the **1** and **4** catalytic systems afforded respectively up to 94 and 99%  $\beta$ -nitroethanol yields (based on benzaldehyde) with an appreciable diastereoselectivity toward the formation of the *anti* isomer (*anti:syn* selectivities 74:26 and 79:21 for **1** and **4**, respectively), which does not change along the reaction time. The palladium compounds **3** and **6** led to similar yields, but the selectivity for one of the isomers was very poor. In fact, *anti:syn* ratios of ca. 50:50 were observed.

The higher catalytic activity for the Ni(II) complex 4, excellent even at room temperature, cannot be rationalized at the moment. The differences in the electrochemical oxidation potentials measured in different solvents, i.e.,  $E_{1/2} = +0.60$  and



**Figure 10.** Yield of  $\beta$ -nitroalkanol obtained from the Henry coupling of benzaldehyde with nitroethane, catalyzed by 1 (dashed lines) or 4 (solid lines).

+0.57 V vs Fc<sup>+</sup>/Fc for 1 and 4, respectively (in DCM; see Figure 4) and  $E_{1/2} = +0.57$  and +0.56 V vs Fc<sup>+</sup>/Fc for 1 and 4, respectively (in ACN; see Figure S23), are not significant, while their optical spectra are very similar (not shown). In addition, the small difference in HOMO–LUMO energy separation for the two complexes of 0.008 eV (Table S2) (4.261 eV for the optimized geometry of the neutral singlet compound 1 and 4.253 eV for complex 4 in DCM) does not explain the markedly higher catalytic efficacy of 4.

The Henry reaction is a powerful tool in modern synthetic chemistry.<sup>76–78</sup> Therefore, significant efforts have been directed toward the development of better synthetic protocols and the improvement of stereochemical outcomes. In recent decades, the classical base-catalyzed procedure has been complemented by metal-catalyzed processes which proceed via various modes of reactant activation depending on the metal, ligand(s), and additives. The metal cation is expected to act as a Lewis acid center, activating nitroalkane (increasing its acidity) and/or aldehyde (increasing its electrophilic character). The ligand or additive, having a Lewis base character, accepts a proton from nitroalkane to generate a nucleophilic nitronate anion. Scheme 3 shows a plausible mechanism for the Henry reaction of benzaldehyde with nitroethane catalyzed by complex 1 or 4.





This mechanism involves the coordination of nitroethane to the Ni(II) center to afford the complex **A** with subsequent proton abstraction from the activated nitroethane by one of the two anionic semicarbazide fragments of the ligand. This cooperative process gives the nucleophilic species **B**, which reacts with benzaldehyde to yield **C**. The latter after the intramolecular proton transfer converts into the final complex **D**.

Recycling of 4 as a catalyst was tested (see the Experimental Section), but the drastic decrease in product yield observed after the second cycle hampered its further reuse.

The catalytic performance of 1 or 4 toward the Henry C–C coupling of benzaldehyde with nitroethane is comparable to, or superior to, those exhibited by other Ni(II) complexes<sup>79–81</sup> under various conditions such as under homogeneous,<sup>79</sup> solvent-free,<sup>80</sup> or ionic liquid<sup>81</sup> conditions. However, the diastereoselectivity obtained in the case of 1 and 4 is different from that shown by recently prepared dinuclear and trinuclear Ni(II) aroylhydrazone complexes<sup>80</sup> that catalyze the Henry coupling of benzaldehyde and nitroethane in methanol at room temperature, with a maximum yield of 72% and a diastereoselectivity toward the formation of the *syn* isomer of 64:36 *syn:anti*. Its improvement required solvent-free conditions (89.2% yield; 72:28 *syn:anti* selectivity) and higher temperatures (75 °C: 90.6% yield; 76:24 *syn:anti* selectivity).

The knowledge<sup>82</sup> that ultrasound (US) can be used as an activation method (by improving yields or selectivity and reducing duration time) to perform chemical reactions led us to test the catalytic activity of compounds 1, 3, 4, and 6 for the Knoevenagel condensation of benzaldehyde and malononitrile under sonochemical conditions. It was found that 1, 3, 4, and 6 are able to selectively catalyze, at room temperature, the above US-assisted reaction to afford 2-benzylidenemalononitrile (Scheme 2). The best reaction conditions, achieved by varying reaction parameters such as time, type of solvent, and ratio of reagents or catalyst amount, are benzaldehyde (1 mmol), malononitrile (2 mmol), 10  $\mu$ mol of 1, 3, 4, and 6, acetonitrile (2 mL) in air, room temperature and under US irradiation for 2 h. Under such conditions, similar yields (up to 56%) of the C-C coupling product (selectivity >99%) were obtained for the above compounds. US irradiation significantly promoted the reaction, allowing us to achieve the same yield in a markedly shorter time (e.g. catalytic system 6 under 2 h of US irradiation led to a 53% yield of 2-benzylidenemalononitrile, whereas only 11% was reached under the same conditions for the non-US-assisted reaction). However, since several homogeneous metal-based catalysts have been reported<sup>83,84</sup> to provide yields higher than those of the present work, further studies were not performed.

### CONCLUSIONS

A reliable multistep procedure for the synthesis of 14membered bis-semicarbazide macrocyclic compounds IX has been developed previously by some of us. However, these potential ligands for transition metals revealed poor solubility in common organic solvents, mainly because of the presence of strong hydrogen bonding involving lactam units in the crystal structure. The low solubility limited their use in complex formation reactions. Alkylation of IX did not result in alkylation of semicarbazide moieties at the oxygen atom. Instead, butylation at one of the hydrazinic NH groups took place, which conferred solubility in common organic solvents due to the lack of hydrogen-bonding interactions typical for IX. A series of six nickel(II), copper(II), and palladium(II) complexes with hexaaza macrocycles  $H_2L^H$  and  $H_2L^{OMe}$  were synthesized and characterized by analytical and spectroscopic techniques (IR, UV-vis, <sup>1</sup>H and <sup>13</sup>C NMR), ESI mass spectrometry, single-crystal X-ray diffraction, and spectroelectrochemistry. EPR spectroelectrochemical experiments with nickel(II) complexes 1 and 4 and DFT calculations indicate the strong noninnocent character of the ligand. Copper(II) complexes 2 and 5, which showed both oxidation and reduction in the available window of potentials, proved to be quite effective catalysts in microwave-assisted neat styrene oxidation in benzaldehvde. Nickel(II) and palladium(II) complexes 1, 3, 4, and 6, which revealed only reversible or quasi-reversible oxidation in the same tested potential range, were found to catalyze the Henry coupling reaction of benzaldehyde with nitroethane. Nickel(II) complexes 1 and 4 provided yields up to 99% and marked diastereoselectivity in the formation of the anti isomer, in comparison to palladium-(II) complexes, which afforded anti:syn ratios of ca. 50:50. In addition, the diamagnetic complexes 1, 3, 4, and 6 catalyzed the Knoevenagel condensation reaction of benzaldehyde and malononitrile to 2-benzylidenemalononitrile under sonochemical conditions at room temperature with yields up to 56%. However, superior yields were reported recently for other homogeneous metal-based catalysts.

#### ASSOCIATED CONTENT

#### **Supporting Information**

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.inorgchem.0c01119.

Atom-labeling scheme used in the NMR resonance assignment, IR, NMR, and ESI mass spectra, fragment of the crystal structure of the Ni(II) complex with *trans*-IX (Ar = Ph), *in situ* spectroelectrochemistry of 2 and 4–6, absorption spectra of 1 and 5 and of NOBF<sub>4</sub> oxidized species, cyclic voltammograms of 1 and 4 and of 2 and 5 in the cathodic region, cyclic voltammograms of 1–6 in the region of the first anodic peak, EPR spectra of 2 and 5, comparison of the experimental and calculated absorption spectra for neutral, one-electron-oxidized, and one-electron-reduced complex 5, and details of the conformations of six-membered rings in 2 and 4–6 and of DFT calculations (PDF)

#### Accession Codes

CCDC 1996061–1996063, 1996065, and 2005715 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/ data\_request/cif, or by emailing data\_request@ccdc.cam.ac. uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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#### Notes

The authors declare no competing financial interest.

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