

Contribution from the Evans Chemical Laboratories,
The Ohio State University, Columbus, Ohio 43210

Reactivity Patterns of Nitrogen Electrophiles with Certain Charge-Delocalized Six-Membered Chelate Rings

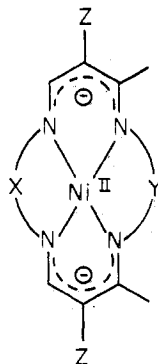
CHRISTIAN J. HIPPI and DARYLE H. BUSCH*

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Several nitrogen electrophiles are observed to react with the carbonyl-substituted central carbon atom in charge-delocalized six-membered chelate rings of macrocyclic nickel(II) complexes. These electrophilic displacement reactions lead to the formation of dinitro species through either nitrosation under oxidizing conditions or direct nitration.

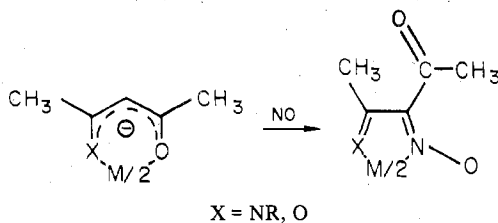
Introduction

Recently, the reactivity toward electrophiles of certain 15-membered macrocyclic complexes of nickel(II) having acetyl-substituted, charge-delocalized six-membered chelate rings has been reported.¹ The novel reactivity patterns observed, including electrophilic alkylation and displacement of the acetyl groups upon protonation of the substituted carbon, prompt us to report the reactions of similar species (Ia, IIa, III, IVa) with nitrogen electrophiles.

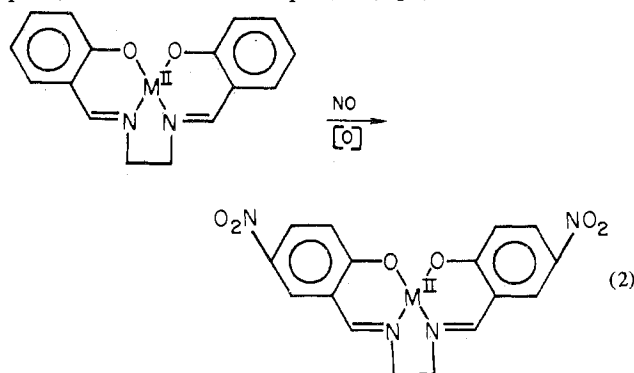


- I, X = C₂H₄, Y = C₃H₆; a, Z = CH₃C(=O)-; b, Z = NO₂
 II, X = (CH₃)₂CCH₂, Y = C₃H₆; a, Z = CH₃C(=O)-; b, Z = NO₂
 III, X = C₂H₄, Y = C₃H₆, Z = -C(=O)OCH₂CH₃
 IV, X = (CH₃)₂CCH₂, Y = C₂H₄; a, Z = CH₃C(=O)-; b, Z = NO₂

Electrophilic substitution reactions with such species, involving the unsubstituted central carbon atom in acetylacetone and acetylacetonimine chelate rings of transition metal complexes, have previously been reported. Nitration of acetylacetone ligands with either dinitrogen tetroxide² or cupric nitrate trihydrate in acetic anhydride³ leads to the formation of nitro-substituted chelate ring products. Nitrosation of labile acetylacetone⁴ or acetylacetonimine complexes,^{2,5,6} however, yielded the isonitroso derivatives (eq 1). Further,



nitrosation under oxidizing conditions with nickel(II)- and copper(II)-bis(salicylaldehyde)-ethylenediimine complexes produced the 5,5'-dinitro species⁷ (eq 2).



In the work reported here, electrophilic displacement reactions with several nitrogen electrophiles have been found to convert the complexes Ia, IIa, III, and IVa to the corresponding dinitro species (Ib, IIb, IVb).

Experimental Section

Materials. All chemicals were reagent grade and were used without further purification. Solvents were stored over molecular sieves for several days prior to use. Elemental analyses for carbon, hydrogen, and nitrogen were all determined by commercial laboratories.

Physical Measurements. Infrared spectra were obtained on Perkin-Elmer Model 337 and 457 recording spectrophotometers and measured in Nujol and hexachlorobutadiene mulls. The nmr spectra were obtained on a Varian A-60A spectrometer at 37° using tetramethylsilane as an internal standard.

6,14-Diacetyl-7,13-dimethyl-1,4,8,12-tetraazacyclopentadeca-4,6,12,14-tetraenatonickel(II) (Ia). This complex was prepared according to literature methods.⁸ Prior to obtaining analytical data the product was recrystallized from chloroform to eliminate the xylene solvent. It forms as red crystals which were washed with ether and dried *in vacuo*. *Anal.* Calcd for NiC₁₇H₂₄N₄O₂: C, 54.40; H, 6.40; N, 14.93. Found: C, 54.27; H, 6.32; N, 14.56.

6,14-Diacetyl-2,2,7,13-tetramethyl-1,4,8,12-tetraazacyclopentadeca-4,6,12,14-tetraenatonickel(II) (IIa). This material was prepared by the method used for Ia, substituting 1,2-diamino-2-methylpropane for ethylenediamine. Recrystallization of the crude product from xylene gave red crystals which were washed with ether and dried *in vacuo*. *Anal.* Calcd for NiC₁₉H₂₈N₄O₂: C, 56.58; H, 6.95; N, 13.90. Found: C, 56.49; H, 6.95; N, 14.00.

6,14-Dicarboxy-7,13-dimethyl-1,4,8,12-tetraazacyclopentadeca-4,6,12,14-tetraenatonickel(II) (III). The linear tetradentate nickel(II) complex was prepared by literature methods⁹ and converted to the macrocycle by refluxing in sufficient anhydrous 1,3-diaminopropane to dissolve the starting material. A typical synthesis involved 20 g of the tetradentate nickel(II) complex, ~50 ml of anhydrous diamine, and 24 hr of reflux. After cooling, the crude product was obtained by addition of water to the reaction mixture, filtered, and dried. Recrystallization from xylene to which ethanol was added to induce

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(2) C. Djordjevic, J. Lewis, and R. S. Nyholm, *J. Chem. Soc.*, **4778** (1962).

(3) J. P. Collman, *Angew. Chem., Int. Ed. Engl.*, **4**, 132 (1965).

(4) D. A. White, *J. Chem. Soc. A*, **233** (1971).

(5) I. Masuda, M. Tamaki, and K. Shinra, *Bull. Chem. Soc. Jap.*, **42**, 157 (1969).

(6) K. S. Bose and C. C. Patel, *J. Inorg. Nucl. Chem.*, **33**, 2947 (1971).

crystallization yielded red crystals which were washed with ether and dried *in vacuo*. Anal. Calcd for $\text{NiC}_{19}\text{H}_{28}\text{N}_4\text{O}_4$: C, 52.41; H, 6.44; N, 12.87. Found: C, 52.13; H, 6.24; N, 12.86.

6,13-Diacetyl-2,2,7,12-tetramethyl-1,4,8,11-tetraazacyclotetradeca-4,6,11,13-tetraenatonickel(II) (IVa). The linear tetradentate nickel(II) complex was prepared as in the synthesis of Ia,⁸ substituting 1,2-diamino-2-methylpropane for ethylenediamine. The macrocycle was prepared by refluxing this complex in anhydrous ethylenediamine for 2 hr. A typical synthesis involved 20 g of the starting material and ~50 ml of ethylenediamine. Longer refluxing results in synthesis of the 14-membered complex with no methyl substituents on the five-membered rings,¹⁰ presumably through diamine exchange. On cooling of the reaction mixture and addition of water the product precipitates. This was filtered, washed with water, dried, and recrystallized from xylene. The resulting orange-red crystals were washed with ether and dried. Several recrystallizations were necessary in order to obtain analytically pure samples. From 20 g of crude recrystallized product, 7 g of IVa were obtained after five recrystallizations. Anal. Calcd for $\text{NiC}_{18}\text{H}_{26}\text{N}_4\text{O}_2$: C, 55.53; H, 6.68; N, 14.40. Found: C, 55.21; H, 6.24; N, 13.97.

6,14-Dinitro-7,13-dimethyl-1,4,8,12-tetraazacyclopentadeca-4,6,12,14-tetraenatonickel(II) (Ib). This complex was prepared by four methods. (1) Ia (1 g) was dissolved in 100 ml of acetonitrile or dichloromethane and flushed with nitric oxide in the presence of air. On standing for several hours the dinitro species separated from solution in 50% yield. (2) Ia (1 g) was suspended in 50 ml of acetonitrile, and stoichiometric quantities of sodium nitrite and then trifluoroacetic acid were added. On addition of the acid the solution immediately darkened as the complex dissolved. After stirring for several hours in the presence of air, the solution volume was reduced to induce crystallization. The yield was found to be essentially quantitative. (3) Ia (1 g) was dissolved in dichloromethane (~50 ml) to which was added excess nitrosyl tetrafluoroborate. On stirring in air the dinitro complex precipitates from solution. (4) III (1 g) was treated with several milliliters of concentrated nitric acid with stirring. After the evolution of gas subsided, the resulting amber solution was diluted with water to 20 ml and neutralized with 6 N sodium hydroxide solution. During the neutralization Ib is formed as an orange precipitate in ~50% yield. Analytical samples were then recrystallized from chloroform, yielding orange crystals. This material was filtered, washed with ether, and dried *in vacuo*. Anal. Calcd for $\text{NiC}_{13}\text{H}_{18}\text{N}_6\text{O}_4$: C, 40.94; H, 4.72; N, 22.03. Found: C, 41.18; H, 4.71; N, 21.91.

6,14-Dinitro-2,2,7,13-tetramethyl-1,4,8,12-tetraazacyclopentadeca-4,6,12,14-tetraenatonickel(II) (IIb). IIb was prepared by methods analogous to methods (1), (2), and (4) for Ia. The crude product was recrystallized from chloroform, washed with ether, and dried *in vacuo*. Anal. Calcd for $\text{NiC}_{18}\text{H}_{26}\text{N}_4\text{O}_4$: C, 44.01; H, 5.38; N, 20.54. Found: C, 44.08; H, 5.34; N, 20.31.

6,13-Dinitro-2,2,7,12-tetramethyl-1,4,8,11-tetraazacyclotetradeca-4,6,11,13-tetraenatonickel(II) (IVb). Complex IVb was prepared by methods analogous to (2) for Ib. The crude material was recrystallized from chloroform, washed with ether, and dried *in vacuo*. Anal. Calcd for $\text{NiC}_{14}\text{H}_{20}\text{N}_6\text{O}_4$: C, 42.53; H, 5.06; N, 21.27. Found: C, 42.42; H, 4.94; N, 21.40.

Results

Complexes Ia, IIa, III, and IVa have been observed to undergo electrophilic displacement reactions with several nitrogen electrophiles to produce the corresponding dinitro species (Ib, IIb, IVb). Thus, nitrosation under oxidizing conditions, with stoichiometric quantities of sodium nitrite and trifluoroacetic acid in acetonitrile, results in almost quantitative yields of the dinitro products. The 15-membered ring products (Ib, IIb) are also readily formed by exposing acetonitrile or dichloromethane solutions of Ia or IIa to nitric oxide in the presence of air. In addition, nitrosyl tetrafluoroborate was observed to convert Ia into Ib in dichloromethane solution under oxidizing conditions. Nitration of the carbonyl-substituted carbons with concentrated nitric acid results in the formation of Ib in good yield and IIb in small amounts from the reactions of III and IIa, respectively.

The products have been characterized by elemental analyses as well as by electronic, infrared, and nmr spectroscopy. The absence of signals corresponding to the protons located on

Table I. Nmr Data for the Complexes^a

| Compd | Obsd spectrum, τ |
|-------|--|
| Ia | 8.15 (quintet ($J \approx 6.5$ Hz), 2 H), 7.70 (s, 6 H, $\text{CH}_3\text{C}(=\text{O})-$), 7.57 (s, 6 H), 6.80 (s, 4 H), 6.32 (t ($J \approx 6.5$ Hz), 4 H), 2.37 (s, 2 H) |
| Ib | 8.17 (quintet ($J \approx 6.5$ Hz), 2 H), 7.57 (s, 6 H), 6.77 (s, 4 H), 6.30 (t ($J \approx 6.5$ Hz), 4 H), 1.71 (s, 2 H) |
| IIa | 8.71 (s, 6 H), 8.23 (quintet ($J \approx$ 6.5 Hz), 2 H), 7.78 (s, 6 H, $\text{CH}_3\text{C}(=\text{O})-$), 7.64 (s, 6 H), 7.06 (s, 2 H), 6.41 (t ($J \approx 6.5$ Hz), 4 H), 1.77 (s, 2 H) |
| IIb | 8.63 (s, 6 H), 8.11 (quintet ($J \approx$ 6.5 Hz), 2 H), 7.55 (s, 6 H), 6.95 (s, 2 H), 6.27 (t ($J \approx 6.5$ Hz), 4 H), 1.77 (s, 2 H) |
| III | 8.67 (t ($J \approx 7$ Hz), 6 H, $\text{CH}_3\text{CH}_2\text{O}-$), 8.20 (quintet ($J \approx 7$ Hz), 2 H), 7.57 (s, 6 H), 6.90 (s, 4 H), 6.35 (t ($J \approx 7$ Hz), 4 H), 5.80 (quartet ($J \approx 7$ Hz), 4 H, $\text{CH}_3\text{CH}_2\text{O}-$), 2.22 (s, 2 H) |
| IVa | 8.64 (s, 6 H), 7.73 (s, 6 H, $\text{CH}_3\text{C}-$ $(=\text{O})-$), 7.59 (s, 6 H), 6.80 (s, 2 H), 6.65 (s, 4 H), 2.38 (s, 1 H), 2.31 (s, 1 H) |
| IVb | 8.59 (s, 6 H), 7.52 (s, 3 H), 7.50 (s, 3 H), 6.73 (s, 2 H), 6.53 (s, 4 H), 1.59 (s, 1 H), 1.55 (s, 1 H) |

^a At 60 MHz; CDCl_3 solution, TMS internal standard.

the carbonyl-containing substituents in their nmr spectra (Table I) and ir bands attributable to the asymmetric and symmetric stretches of the nitro groups at ~1480 and 1275 cm^{-1} , respectively,² are diagnostic of the products. In addition the visible absorption spectra of these materials in chloroform solution all display a shoulder at ~20,000 cm^{-1} (ϵ ~700-1900) and a higher energy charge-transfer band [Ib, 24,040 cm^{-1} (ϵ 39,300); IIb, 24,240 cm^{-1} (36,330); IVb, 23,810 cm^{-1} (36,600)]. Also, the mass spectrum of Ib shows the expected parent ion isotopic peaks (m/e 380 and 382, ratio 2.6:1).

Discussion

Reaction with nitrogen electrophiles at the carbonyl-substituted carbons of Ia, IIa, III, and IVa to produce the dinitro materials can be contrasted with electrochemical oxidation.¹¹ The site of the electron density affected appears to be different in the two reactions. In the former case, electrophilic attack occurs at the central carbon atom of the charge-delocalized six-membered chelate rings while in the latter case the central metal ion is oxidized. The isolation of the dinitro products thus provides evidence for the nucleophilic behavior of these substituted γ -carbon atoms.

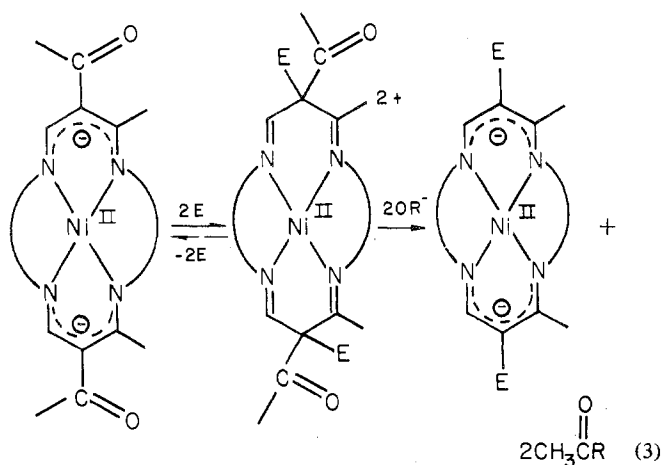
The intermediacy of nitroso groups in the formation of the dinitro products with nitrosating agents under oxidizing conditions is indicated by the products obtained with these reagents in their reactions with labile acetylacetonimine nickel(II) complexes. Nitric oxide,⁴ nitrosyl chloride,² and nitrite ion^{2,4} all produce isonitroso complexes (eq 1). In the nitrosation of Ia, IIa, and IVa the ligand structure cannot rearrange without cleavage of C-C or C-N bonds. Consequently, the nitroso group is not stabilized by coordination to the metal ion.^{2,4} Oxidation of these groups under the reaction conditions then leads to the formation of the observed products. Oxidative nitrosation is also observed in the reaction of nitric

(11) E. S. Gore, F. V. Lovechio, and D. H. Busch, unpublished results.

oxide with nickel(II)- and copper(II)-bis(salicylaldehyde)-ethylenediimine complexes (eq 2). Here, the presence of the transition metal ion activates the aromatic rings toward attack by NO as is seen in the failure of the free ligand to react under equivalent reaction conditions.

The reaction products observed parallel those found for activated aromatic rings,¹² including both carbon nitrosation with subsequent oxidation and nitration under relatively mild conditions. The effect of the carbonyl-containing substituents is shown by the reactions of the analogous deacylated 15-membered ring complexes¹ which do not produce the di-nitro species under the conditions employed in this work.

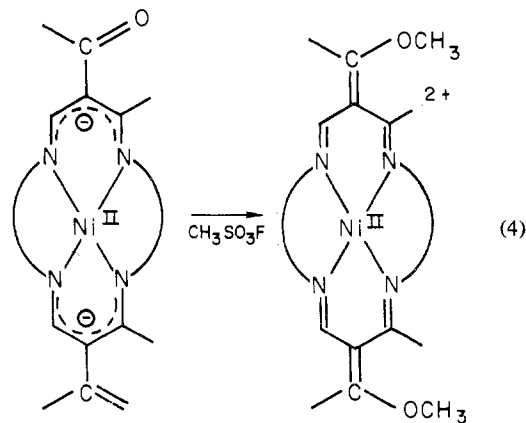
Perhaps the simplest example of electrophilic substitution among these complexes involves their reaction with acids. Jager¹⁰ showed that the corresponding 14-membered complexes can be reversibly protonated at the γ carbons. We have previously reported that protonation of the 15-membered ring complexes is followed by displacement of the acetyl groups of Ia or IIa when the process is carried out in nucleophilic solvents.¹ In a separate study which is designed to model the behavior of the enzyme chloroperoxidase,¹³



(12) P. B. D. DeLaMare and J. H. Ridd, "Aromatic Substitution, Nitration, and Halogenation," Academic Press, New York, N. Y., 1959.

it has also been found that the Br^+ group can be added reversibly to the γ carbons in the six-membered chelate rings of complexes of this class. The brominated derivatives were isolated and subsequently allowed to react with suitable substrates. In these reactions the Br^+ group is transferred. We conclude that the first step (addition) in electrophilic displacement occurs with a variety of electrophiles. Nucleophilic attack on the substituent on the resulting tetrahedral carbon leads to displacement of either the carbonyl-containing function or the electrophile (eq 3).

A similar reaction sequence is seen in the electrophilic attack of alkylating agents on the carbonyl oxygen atoms of these γ -carbon-substituted, charged rings, leading to the formation of the novel vinyl ether species¹ (eq 4), whose struc-



ture has been determined crystallographically by Corfield and Mokren.¹⁴

Registry No. Ia, 38402-68-5; Ib, 38402-69-6; IIa, 38402-70-9; IIb, 38402-71-0; III, 38402-72-1; IVa, 38402-73-2; IVb, 38402-74-3.

Acknowledgment. This work was supported by National Institutes of Health Grant GM 10040 from the National Institute of General Medical Sciences.

(13) C. J. Hipp and D. H. Busch, unpublished results.

(14) P. W. R. Corfield and J. D. Mokren, unpublished results.