Synthesis of β-Substituted Tetramethyltetraazacyclotetradecatetraene and Its Metal(II) Complexes

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N,N'-Bis(1-methyl-3-thioxo-1-butenyl)ethylenediamine (**3**) was prepared by the reaction of *N,N'*-bis(1-methyl-3-oxo-1-butenyl)ethylenediamine with phosphorus pentasulfide in pyridine. The reaction of **3** with ethylenediamine gave 5,7,12,14-tetramethyl-1,4,8,11-tetraazacyclotetradeca-4,6,11,13-tetraene (**4**) in a 46% yield. The reactivity of the β positions of **4** and its metal(II) complexes (M=Cu, Ni, Pd) toward various electrophilic reagents was explored, and some β,β'-bissubstituted tetraaza macrocyclic compounds (substituent=Cl, $SC_6H_4NO_2$(o), N_2Ph) and their metal complexes were prepared, respectively. The former also reacted with metal(II) acetates to afford the same metal complexes.

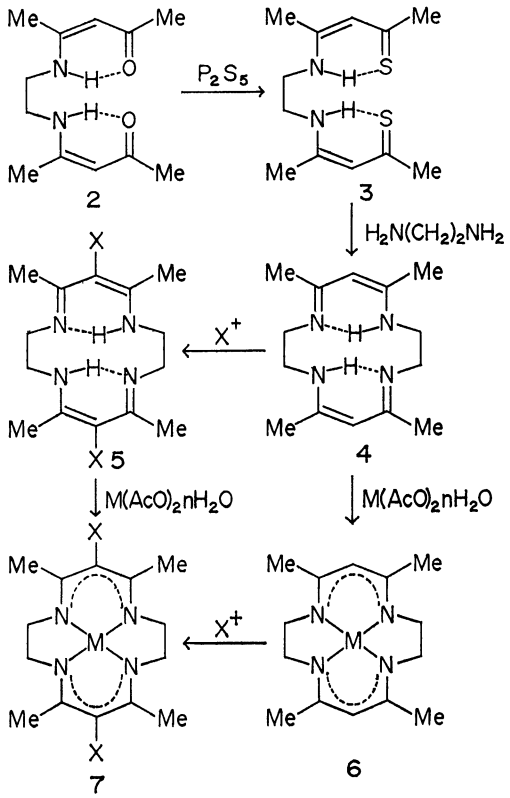
The preparations and reactivities of tetraaza macrocycles and their metal complexes containing enamino imines conjugated systems have attracted considerable attention as models for natural tetraaza macrocycles, such as porphyrins and corrins. It is also interesting to elucidate the reactivity of the β positions of their macrocyclic ligands and metal complexes. Fischer *et al.*[1] have reported that the β positions of 5,14-dihydrodibenzo[*b,i*][5,9,14,18]tetraaza[14]annulene (**1**) react with *p*-chlorobenzenediazonium salt to give a 7,16-bis(*p*-chlorophenylazo)substituted derivative. The reaction of **1** with ethyl 1-chloro-3,3-dicyanopropenoate has also been found to yield a 7,16-bis(ethoxycarbonyl)-substituted derivative.[2] While nickel(II) complex of **1** reacted with bromine to give an octabromo derivative substituted into benzene nuclei.[2] Holm *et al.*[3] have found that some β,β'-bisphenylated macrocycles are prepared by the reaction of 4-phenyl-1,2-dithiolium salt with diamine. Jäger[4] has also reported the template synthesis of some macrocyclic metal complexes with COR or COOR groups at the β positions. This cyclization appears dependent on the presence of a carbonyl-containing group.[5] The macrocycle, 5,7,12,14-tetramethyl-1,4,8,11-tetraazacyclotetradeca-4,6,11,13-tetraene (**4**), without the substituents at the β positions has been prepared by the reaction of ethylenediamine with 4-amino-2-ethyl-2-oxonia-3-pentene[3b,5] and/or *N,N'*-bis(1-methyl-3-thioxo-1-butenyl)ethylenediamine (**3**), which is prepared from *N,N'*-bis(3-ethyl-3-oxonia-1-methyl-1-butenyl)ethylenediamine and sodium hydrogensulfide.[3a,6] In all these preparations, triethyloxonium tetrafluoroborate is required as a catalyst, and the yield is generally low.

We synthesized **4** without using the specific and expensive catalyst, and elucidated the electrophilic substitution reactivity of the β positions of the free ligand, **4**, and its metal(II) complexes (**6**).

Results and Discussion

The compound, **3**, was synthesized by means of reaction of *N,N'*-bis(1-methyl-3-oxo-1-butenyl)ethylenediamine (**2**) with phosphorous pentasulfide in pyridine in a 34% yield. The macrocycle, **4**, was obtained in the highest yield (46%) when **3** was refluxed with an equimolar amount of ethylenediamine in benzene for 24 h. By these reactions, **4** could be synthesized without using the expensive and specific catalyst.

The macrocycle, **4**, reacted with *N*-chlorosuccinimide (NCS) of 2.2 molar ratio at 5 °C in the dark under a nitrogen atmosphere to give 6,13-dichloro-5,7,12,14-tetramethyl-1,4,8,11-tetraazacyclotetradeca-4,6,11,13-tetraene (**5a**) in a 25% yield; the addition of 4.4 molar ratio gave 6,6,13,13-tetrachloro-5,7,12,14-tetramethyl-1,4,8,11-tetraazacyclotetradeca-4,7,11,14-tetraene (**8**) in a 42% yield. Under these conditions, it is considered that the reactions proceed by an ionic mechanism. Their structure was established by analytical and spectral data. That is to say, the NMR spectrum of **5a** showed the same pattern as that of **4**, except that absorption of –CH= protons in the vicinity of 4.5 ppm was missing. That of **8** also lacked the absorptions for –CH= and NH protons, and the protons of four CH_3 and four



a: X=Cl, **b**: X=$SC_6H_4NO_2$(*o*)
c: X=N_2Ph, **d**: X=COPh
M: Cu, Ni, Pd

Table 1. Melting points and analytical data of the products

Compound	Mp/°C	Found (%)				Calcd (%)			
		C	H	N	Cl or S	C	H	N	Cl or S
5a	178—179	52.91	7.07	17.56	22.27	53.00	6.99	17.66	22.35
5b	224	56.02	5.39	14.96	11.42	56.29	5.45	15.15	11.56
5c	218—219	68.22	7.04	24.27		68.39	7.26	24.54	
6Pd	310—312	47.81	6.26	15.90		47.67	6.28	15.88	
7bCu	194	50.53	4.50	13.75	10.24	50.68	4.58	13.64	10.40
7bNi	198	51.03	4.52	13.61	10.41	51.08	4.61	13.74	10.49
7bPd	204—205	47.50	4.30	12.58	9.60	47.38	4.28	12.75	9.73
7cCu	277—278	60.34	5.78	21.40		60.27	5.83	21.62	
7cNi	275—276	60.83	5.79	21.83		60.84	5.89	21.83	
7cPd	271—272	55.59	5.31	19.76		55.67	5.39	19.97	
7dNi	250—251	56.59	5.71	10.92		56.53	5.89	10.91	
7dPd	267—268	60.02	5.23	9.98		59.95	5.39	9.98	
8	154	43.52	5.15	14.29	36.47	43.54	5.22	14.50	36.72

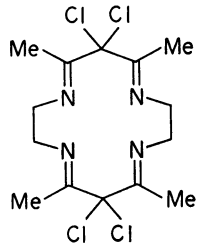
Table 2. Spectral data of the products

Compound	IR[a] $\tilde{\nu}$/cm^{-1}				NMR[b] δ				UV[c] λ_{max}/nm($10^{-3}\varepsilon$)
	νNH or νC=O	νC=C+ νC=N	δNH or $\nu_{as}NO_2$	ν_sNO_2	CH_3	CH_2–CH_2	X	NH	
4	3200	1620	1568[c]		1.88(s)	3.45(s)	4.51(s)	11.5[d]	297(33.2)[e]
5a	3200	1607	1560[c]		2.13(s)	3.58(s)		11.7[d]	252(2.4), 308[sh](17.2), 317(21.8), 350(4.7)[e]
5b	3200	1590	1565 1515	1337[c]	2.18(s)	3.60(s)	7.4—8.3(m)	13.2[d]	307(20.7), 381(8.0)
5c	3200	1586	1576[c]		2.20(s)	3.50(s)	7.1—7.5(m)	—[f),g]	296(14.5), 335(26.5), 375(29.2), 420[sh](17.6)
6Pd		1554			2.01(s)	3.53(s)	4.70(s)		282(9.9), 300[sh](7.2), 346(4.6), 367[sh](4.8), 395(6.0), 412(6.3), 459(0.9), 488(1.0)
7bCu		1563	1517	1331					271[sh](30.0), 335(17.6), 382[sh](10.6), 470[sh](2.4), 570(0.6)
7bNi		1561	1518	1340	2.16(s)	3.23(s)	7.1—8.2(m)		281(32.8), 386(14.0), 470(2.2), 560[sh](1.4)
7bPd		1563	1515	1322	2.30(s)	3.65(s)	7.2—8.3(m)		275[sh](29.2), 388(15.0), 480(1.7)
7cCu		1560							290[sh](4.6), 349(21.8), 400[sh](25.0), 465(40.0), 560[sh](2.6)
7cNi		1553			—	—	—[h]		296[sh](13.0), 373(21.6), 485(40.0)
7cPd		1571			—	—	—[h]		288[sh](6.0), 387(17.8), 489(39.0)
7dNi	1625	1537			1.83(s)	3.35(s)	7.5—8.1(m)		280(18.4), 396(9.0), 420(8.9), 445[sh](7.8), 550[sh](1.6)
7dPd	1626	1539			1.93(s)	3.60(s)	7.5—8.1(m)		280(13.0), 408(9.5), 418[sh](9.3), 440[sh](8.0)

a) KBr. b) $CDCl_3$. c) $CHCl_3$. d) Center of broad signal. e) EtOH. f) DMSO-d_6. g) Not observed. h) Could not be detected because of slight solubility in solvents. s: Singlet. m: Multiplet. sh: Shoulder.

–CH_2– were equivalent and appeared as singlets. The IR spectrum in 1600 cm^{-1} region of **8** showed only one strong absorption at 1660 cm^{-1}, which was assigned to νC=N.[7] The mass spectrum showed the parent ion peak at *m/e* 384, and the UV spectrum exhibited an absorption maximum at 250 nm (ε, 580). This shows that **8** does not have a conjugated system. Compound **8** may be formed by Cl^+ attacking at the 6- and 13-

positions of **5a**, followed by the elimination of NH protons, analogously to the gem-dibromination of the β position of 1,4-diazepines.[8] The melting points, analytical data, and spectral data for the products are presented in Tables 1 and 2.



8

The reaction of **4** with *o*-nitrobenzenesulfenyl chloride in acetonitrile in the presence of triethylamine gave 5,7,12,14-tetramethyl-6,13-bis(2-nitrophenylthio)-1,4,8,-11-tetraazacyclotetradeca-4,6,11,13-tetraene ((**5b**) in a 25% yield. The NMR spectrum showed multiplet absorption for aromatic protons of 8H amount, and the IR spectrum showed strong absorptions at 1515 and 1337 cm^{-1}, which were assigned to $\nu_{as}NO_2$ and ν_sNO_2, respectively.

Compound **4** also reacted with benzenediazonium salt to give 5,7,12,14-tetramethyl-6,13-bis(phenylazo)-1,4,8,11-tetraazacyclotetradeca-4,6,11,14-tetraene (**5c**) in a 61% yield. Because this material is slightly soluble in $CDCl_3$, DMSO-d_6, pyridine-d_5, *etc.*, the NMR signal of NH protons of **5c** could not be detected. However, the IR spectrum showed a weak absorption centered at 3200 cm^{-1}, which was assigned to the intramolecular hydrogen bonded νNH, and showed no absorptions for the non-conjugated νC=N in the region of 1640—1690 cm^{-1}.[1,7] In contrast with the coupling product of **1**, which appears to exist as a hydrazo tautomer,[1] these results suggest that **5c** exists in a chelated azo form.

The metal(II) complexes, **6** (M=Cu, Ni, Pd), of **4** reacted with *o*-nitrobenzenesulfenyl chloride in the presence of pyridine to give 6,13-bis(2-nitrophenylthio)-substituted metal complexes (**7b**) in 83% (M=Ni) and 61% (M=Pd) yield, respectively, and **6** (M=Cu) gave decomposition products.

The reaction of **6** (M=Cu, Ni, Pd) with benzenediazonium salt also gave 6,13-bis(phenylazo)-substituted metal complexes (**7c**) in 53% (M=Cu), 97% (M=Ni) and 89% (M=Pd) yield, respectively.

The reaction of **6** (M=Ni, Pd) with benzoyl chloride in the presence of pyridine gave 6,13-dibenzoyl-substituted metal complexes (**7d**) in 57% (M=Ni) and 62% (M=Pd) yield, respectively, and **6** (M=Cu) also gave decomposition products. The structure of **7d** (M=Ni, Pd) was established as follows: the IR spectrum showed νC=O at 1625 and 1626 cm^{-1}, and NMR spectrum showed multiplet absorptions for 10H aromatic protons at 7.5—8.5 ppm; there was no absorption of the methine protons.

The free ligands, **5b** and **5c**, reacted with the metal(II) acetates (M=Cu, Ni, Pd) in DMF and/or DMSO to yield the corresponding metal complexes **7b** and **7c** in 79—90% yield, respectively. The complexation of **5a** gave decomposition products. The structures of these products were confirmed by direct comparison of the spectral data with the corresponding products derived from **6b** and **6c** and mixed examination. The **7b** (M=Cu), which could not be obtained by the reaction of **6** (M=Cu) with *o*-nitrobenzenesulfenyl chloride, was easily obtained by the reaction of **5b** with copper acetate in a 81% yield.

Attempts to synthesize other β,β'-disubstituted derivatives of **4** and **6** such as 6,13-dinitro-, 6,13-dibromo-, 6,13-diiodo-, 6,13-diformyl-, and 6,13-dithiocyano-derivatives were all unsuccessful, and **4** and **6** gave decomposition products, respectively. It thus appears that the substrates or products are unstable under these reaction conditions.

It is considered that the electrophilic reactivity of the β positions of the free ligand, **4**, and its metal(II) complexes, **6**, which are stabilized by the delocalization of π-electrons, may be attributed to their meneidic or regenerative character, as well as that of enamino ketones,[9] vinamidines and its salts[10] and the metal complexes of β-diketones.[11]

The IR spectra for the free ligands, **5a**, **5b**, and **5c**, show a broad absorption at 3200 cm^{-1} and a strong absorption at 1560—1576 cm^{-1} which are associated with νNH and δNH by the shift to lower frequencies owing to the replacement of active protons by deuterium ions. A strong absorption observed in the range of 1586—1607 cm^{-1} may be assigned to the νC=C+νC=N, which shift into the range of 1553—1571 cm^{-1} upon complex formation. The νC=O of the β-substituents and the νC=C+νC=N for the chelate rings of **7d** (M=Ni, Pd) are observed in both lower frequencies at 1625 or 1626 cm^{-1} and at 1537 or 1539 cm^{-1}, respectively. This seems to indicate that the β,β'-dicarbonyl groups have highly conjugated with the chelate rings.

The NMR spectra for the free ligands, **5a**, **5b**, and **5c**, show a broad signal of NH protons at 11.7 and 13.2 ppm except **5c**, and a sharp singlet of N–CH_2– and C–CH_3 at 3.50—3.60 ppm and at 2.13—2.20 ppm, respectively. The signals of the N–CH_2– and the C–CH_3 for the metal complexes also are sharp singlets. These results, together with the results from the IR spectra, have shown that these free ligands exist in an intramolecular hydrogen bonded chelate structure, which seems to be symmetric structure delocalized of π-electrons through the enamino imine conjugation[12] analogous to their metal complexes.

The visible and UV spectra of the free ligands, **5a**, **5b**, and **5c**, display two—four absorption bands in the range of 250—420 nm. The spectral features for these metal complexes are more complicated, and **7b** and **7c** (M=Cu, Ni, Pd) exhibit one or two new absorption peaks in the range of 466—570 nm, which may be assigned to π-π^* transitions within a ligand molecule and/or charge-transfer transitions. **7d** (M=Ni, Pd) also exhibit two or three similar absorption peaks in the range of 418—550 nm.

Experimental

The Schiff base, *N,N'*-bis(1-methyl-3-oxo-1-butenyl)ethylenediamine (**2**) was prepared according to the method of Martell *et al.*[13] The IR, NMR, and UV spectra were

recorded with JASCO IRG, Hitachi R24B, and Hitachi 124 spectrometers respectively. The mass spectra were determined with a JEOL JMS-D100 mass spectrometer. All the melting points are uncorrected.

Preparation of **3**: To a solution of **2** (22.4 g, 0.1 mol) in pyridine (50 ml) was slowly added powdered phosphorus pentasulfide at room temperature. The reaction mixture was stirred for 5 h, and then poured into 2 l of water. The mixture was neutralized by sodium hydrogencarbonate and filtrated. The residue was recrystallized with ethanol to give 8.8 g (34%) of **3**; mp 152—153 °C. Found: C, 56.15; H, 8.05; N, 10.77; S, 24.75%.

Preparation of **4**: A solution containing **3** (5.1 g, 20 mmol) and ethylenediamine (1.2 g, 20 mmol) in benzene (120 ml) was refluxed for 24 h. Removal of solvent, addition of ethanol, filtration, and recrystallization from ethanol gave 2.3 g (46%) of **4**; mp 223—224 °C (lit,[5] mp 226—228 °C, yield 15%).

Reaction of **4** *with NCS*: To a soution of **4** (1.24 g, 5 mmol) in chloroform (10 ml) was added NCS (1.5 g, 11 mmol) under a nitrogen atmosphere in the dark at 5 °C and stirred for 1 h. The resulting succinimide was removed by filtration, and the filtrate was evaporated to dryness under reduced pressure. The residual solid was recrystallized with ethanol to give 0.4 g (25%) of **5a**; MS *m/e*: 316 (M^+). The melting points, analytical data, and spectral data for the products were tabulated in Tables 1 and 2. The addition of 3.0 g (22 mmol) of NCS gave **8** in a 42% yield (from EtOH); MS *m/e*: 384 (M^+).

Preparation of **5b**: To a solution of **4** (2.5 g, 10 mmol) and triethylamine (3.0 g, 30 mmol) in acetonitrile (100 ml) was slowly added a solution of *o*-nitrobenzenesulfenyl chloride (4.2 g, 22 mmol) in acetonitrile (30 ml) under a nitrogen atmosphere, and then refluxed with stirring for 3 h. The reaction mixture was poured into water, and the resulting precipitation was separated by filtration. The products were isolated by column chromatography on silica gel ($CHCl_3$) to give 1.4 g (25%) of **5b**; MS *m/e*: 554 (M^+).

Preparation of **5c**: To 30 ml of a solution, neutralized by sodium acetate, containing 11 mmol of benzenediazonium chloride, was added a diluted acetic acid solution containing 1.2 g (5 mmol) of **4** with stirring at 5 °C. This mixture was then stirred for 2 h at this temperature and for 2 h at room temperature. The reaction mixture was poured into water, and filtrated. The collected solid was recrystallized with DMF to give 1.4 g (61%) of **5c** as yellow powder; MS *m/e*: 456 (M^+).

Preparation of the Metal(II) Complexes, **6**, *of* **4**: Copper(II) and nickel (II) complexes of **4** were synthesized by the method of Holm *et al.*[5] Palladium(II) complex was synthesized by the reaction of equimolar amounts of palladium acetate and **4** in hot ethanol; yield 74% (from $CHCl_3$).

General Procedure for the Reaction of **6** *with* o-*Nitrobenzenesulfenyl Chloride*: To a solution of **6** (5 mmol) and pyridine (11 mmol) in chloroform (150 ml) was added *o*-nitrobenzenesulfenyl chloride (11 mmol) under a nitrogen atmosphere at room temperature, and refluxed for 4 h. The reaction mixture was evaporated *in vacuo*, and recrystallization of the residue from solvent afforded the corresponding **7b**. **7b** (M=Ni): yield 83% (from benzene). **7b** (M=Pd): yield 61% (from $CHCl_3$–EtOH).

General Procedure for the Reaction of **6** *with Benzenediazonium Salt*: To an aqueous solution (100 ml) containing benzenediazonium chloride (11 mmol) and neutralized with sodium acetate, was slowly added a diluted acetic acid solution (80 ml) of **6** (5 mmol) at 5 °C; the mixture was then stirred at room temperature for 2—3 h. The reaction mixture was poured into water, and the resulting precipitate was removed by filtration and washed with ethanol. The product was purified by stirring with about 20 times of DMF. **7c** (M=Cu): yield 53%. **7c** (M=Ni): yield 97%. **7c** (M=Pd): yield 89%.

General Procedure for the Reaction of **6** *with Benzoyl Chloride*: To a solution of **6** (2 mmol) and pyridine (4.4 mmol) in dichloromethane (100 ml) was added benzoyl chloride (4.4 mmol) at room temperature, and the mixture was refluxed for 4 h. After removal of the solvent, the residue was recrystallized. **7d** (M=Ni): yield 57% (from $CHCl_3$–EtOH). **7d** (M=Pd): yield 62% (from $CHCl_3$).

Complexation of **5**: The free ligands, **5**, reacted with the metal(II) acetates of a small excess in DMF and/or DMSO for 15 min at 120 °C to give the corresponding metal complexes **7**. **7b** (M=Cu): yield 81% (from DMF). **7b** (M=Ni): yield 98% (from benzene). **7b** (M=Pd): yield 81% (from $CHCl_3$–EtOH). **7c** (M=Cu): yield 90%. **7c** (M=Ni): yield 88%. **7c** (M=Pd): yield 79%. The complexations of **5a** gave decomposition products.

Other Electrophilic Substitutions: The compounds, **4** and **6**, reacted with acetic anhydride and nitric acid or copper nitrate, *N*-bromosuccinimide, *N*-iodosuccinimide, bromine, Vilsmeier reagent, thiocyanogen, *etc.*, to give products which decomposed during the reactions or the separations.

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