norcanrenone.[3b,10] Treatment of *dl*-canrenone (**17**) with thiolacetic acid[3b] provided, in 65% yield, *dl*-spironolactone (**19**),[6a,7a,c] mp 203–207 °C.[7d] This material was identified by comparison[9] with authentic spironolactone.[3b] Similarly *dl*-**18** was converted into *dl*-19-norspironolactone (**20**),[6b,7a,c] mp 209–219 °C (57% yield), which was identified by comparison[9] with authentic material.[3b] It is noteworthy that the 19-norsteroidal lactones are generally more potent as aldosterone blocking agents, but less readily accessible by partial synthesis, than the normal compounds.[3a]

Acknowledgment. We are indebted to the National Institutes of Health, the National Science Foundation, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research. D.J.D. was the recipient of an NIH Postdoctoral Fellowship, and D.B. was supported by a fellowship from the Swiss National Science Foundation.

We also thank Dr. William F. Johns of the G. D. Searle Co. for arranging for us to receive the various authentic specimens of spironolactone and related substances that were used in this study.

Registry No. (±)-**5**, 81740-48-9; (±)-**6**, 81740-49-0; (±)-**7**, 81768-94-7; (±)-**8**, 81768-95-8; (±)-**9**, isomer 1, 81768-96-9; (±)-**9**, isomer 2, 81768-97-0; (±)-**10**, isomer 1, 81768-98-1; (±)-**10**, isomer 2, 81768-99-2; (±)-**11**, 81769-00-8; (±)-**12**, 81769-01-9; (±)-**13**, 81769-02-0; (±)-**14**, 81769-03-1; (±)-**15**, 81769-04-2; (±)-**16**, 81769-05-3; (±)-**17**, 81769-06-4; (±)-**18**, 81769-07-5; (±)-**19**, 81769-08-6; (±)-**20**, 81769-09-7.

(10) In work to be reported in detail elsewhere, the ketone **12**, on submission to the ozonolysis–cyclodehydration–elimination sequence (cf. **14** → **16** → **18**) afforded the dienedione (**18** with a 17-keto group in place of the lactone), which on selective hydrogenation of the 6,7 double bond was converted into *dl*-estr-4-ene-3,17-dione (Scott, J. W.; Saucy, G. *J. Org. Chem.* **1972**, *37*, 1652–1658), identified by comparison (ref 9) with authentic material.

Total Synthesis of (−)-Domoic Acid. A Revision of the Original Structure

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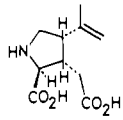
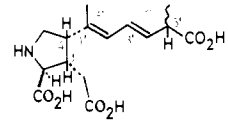
Received February 1, 1982

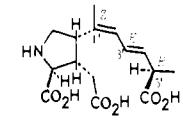
(−)-Kainic acid[1] (**1**) has attracted considerable interest in recent



1



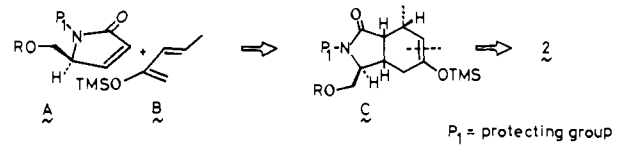
2



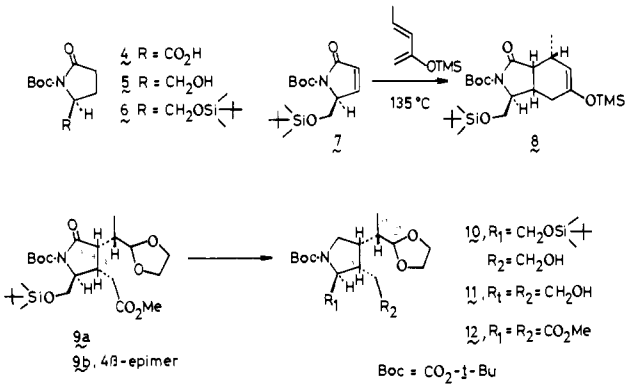
3

years owing to its potent neurotransmitting activity in the central nervous system.[2] The related structure **2**, with undefined stereochemistry at C-5′, was assigned[3a] to (−)-domoic acid[3b] isolated from the red algae *Chondria armata* Okamura (Rhodomelaceae) ("hanayanagi" or "domoi" in Japanese). Although domoic acid was known to exhibit similar neurobiological activities, only preliminary tests could be carried out owing to the extreme scarcity of sample available from marine sources; moreover, the algae itself has been depleted during the last decade. The synthesis of the proposed structure **2** was carried out for the aftermentioned reasons as well as to determine the C-5′ configuration. However, since neither of the synthetic C-5′ epimers corresponded to natural domoic acid, an X-ray crystallographic study of domoic acid was carried out, and this showed that the side chain had in fact the 1′*Z*,3′*E*,5′*R* stereochemistry (*ZER*)-**3**.[4] In the following we report the total synthesis of natural (−)-domoic acid (**3**) together with its *EER* and *EES* isomers **2**.

Scheme I



Scheme II



The synthesis was designed on the assumption that a [4 + 2] cycloaddition of **A** and **B** should lead to amide **C** for steric as well as electronic reasons[5] (Scheme I).

N-tert-Butoxycarbonyl-L-pyrroglutamic acid (**4**)[6] derived from L-glutamic acid was converted into the alcohol **5**:[7,8] (i) $ClCO_2Et/Et_3N/THF$, −10 °C; (ii) $NaBH_4$/90% EtOH, −10 °C. The silyl ether **6**[8] [oil, $[\alpha]^{25}_D$ −61° (*c* 1.1, $CHCl_3$)], obtained by reacting **5** with *tert*-butyldimethylsilyl chloride/DMF/imidazole, was converted into the unsaturated amide **7**[8] by the selenenylation–deselenenylation procedure [(i) LDA/THF/PhSeCl, −78 °C; (ii) O_3/CH_2Cl_2, −78 °C, NaOAc (powder), 0 °C] in 70% yield from **4**; mp 64–65 °C, $[\alpha]^{25}_D$ −176° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.26 (dd, *J* = 2, 7 Hz, 3-H), 6.12 (dd, *J* = 1.5, 7 Hz, 4-H), 4.60 (m, 2-H), 4.15 (dd, *J* = 4, 10 Hz, 2-CH_2OSi), 3.71 (dd, *J* = 7, 10 Hz, 2-CH_2OSi), 1.59 (s, *t*-BuO). The fact that no racemization had occurred during the last two steps was ascertained by hydrogenation of **7** to the starting material **6** (H_2/Pd–C, AcOEt), which exhibited the same specific rotation. Cycloaddtion of 2-(trimethylsilyl)oxy-1,3-pentadiene (prepared from *trans*-3-pentene-2-one/LDA/trimethylsilyl chloride, −78 °C; bp 150–153 °C)[9] to the pyrrolone **7** in toluene (135 °C, sealed tube, 3 days) proceeded stereospecifically to afford the single adduct **8**. The optical purity of **8** was checked by recovering unreacted starting material **7** after a 24-h reaction period and

(1) Structure: Murakami, S.; Takemoto, T.; Tei, Z.; Daigo, K. *J. Pharm. Soc. Jpn.* **1955**, *75*, 869. Synthesis: (a) Ueno, Y.; Tanaka, K.; Ueyanagi, J.; Nawa, H.; Sanno, Y.; Honjo, M.; Nakamori, R.; Sugawa, T.; Uchibayashi, M.; Osugi, K.; Tatsuoka, S. *Proc. Jpn. Acad.* **1957**, *33*, 53. (b) Oppolzer, W.; Andres, H. *Helv. Chim. Acta* **1979**, *62*, 2282.

(2) (a) Johnston, G. A. R.; Curtis, D. R.; Davis, J.; McCulloch, R. M. *Nature (London)* **1974**, *248*, 804. (b) Coyle, J. T.; Schwarz, R. *Ibid.* **1976**, *263*, 244. (c) McGeen, E. G.; McGeen, P. L. *Ibid.* **1976**, *263*, 517. (d) Shinozaki, K. "Kainic Acid as a Tool in Neurobiology"; Raven Press: New York, 1978.

(3) (a) Takemoto, T.; Daigo, K.; Kondo, Y.; Kondo, K. *J. Pharm. Soc. Jpn.* **1966**, *86*, 874. (b) Daigo, K. *Ibid.* **1959**, *79*, 350–365.

(4) Nomoto, K.; Iwashita, T.; Ohfune, Y.; Takemoto, T.; Daigo, K. to be submitted for publication.

(5) Vedejs, E.; Gadwood, R. C. *J. Org. Chem.* **1979**, *43*, 376.

(6) Schröder, E.; Krieger, K. *Justus Liebigs Ann. Chem.* **1964**, *673*, 196.

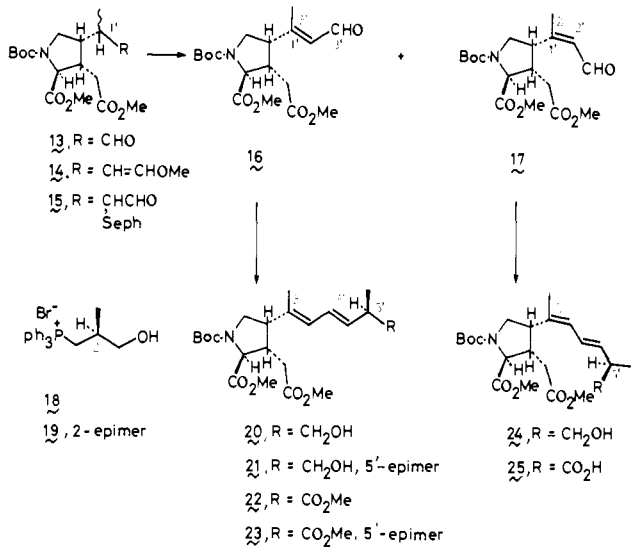
(7) Some racemization was encountered during the reduction of **4**, the resultant alcohol **5** having an $[\alpha]_D$ value of −57°. Removal of the racemate by recrystallization (acetone/hexane 1:20) afforded the optically pure **5** [70% conversion; mp 98–99 °C; $[\alpha]^{25}_D$ −63° (*c* 0.61, $CHCl_3$)], from the mother liquid. The conversion of **5** obtained in this manner to the starting material **4** with PDC/DMF led to optically pure material [$[\alpha]^{25}_D$ −35° (*c* 1.0, AcOH); (lit.[6] $[\alpha]^{25}_D$ −35° (AcOH))].

(8) Satisfactory spectroscopic data and elementary analyses were obtained.

(9) A regiospecific enolate formation of *trans*-3-penten-2-one has been reported: Stork, G.; Kraus, G. A.; Garcia, G. A. *J. Org. Chem.* **1974**, *39*, 3459.

0002-7863/82/1504-3511$01.25/0

Scheme III



showing that the optical activity remained unchanged.

Adduct **8** (Scheme II), without isolation, was submitted to the following three-step sequence: (i) O_3/CH_2Cl_2, −78 °C, dimethyl sulfide (DMS), room temperature, 6 h; (ii) CH_2N_2; (iii) 2-methyl-2-ethyl-1,3-dioxolane/*p*-TsOH, room temperature, 3 h. This yielded **9a**[8,10] [oil, $[\alpha]^{25}_D$ −39.3° (*c* 0.56, $CHCl_3$), 40% from **7**, accompanied by 8% of the 4β-isomer **9b**[8]]. The amide function was reduced at this stage in the presence of multifunctional groups, *especially the ester group attached to the amide nitrogen.* After several unsuccessful attempts with hydride reagents, this was achieved[11] in 70% yield by employment of the borane–dimethyl sulfide complex (BH_3·DMS) to give **10**[8] [oil; $[\alpha]^{25}_D$ −22.7° (*c* 0.9, $CHCl_3$); IR ($CHCl_3$) 3450, 1680 cm^{-1}; the reaction was accompanied by a simultaneous reduction of the C-3 ester group to an alcohol[12]]. Selective deprotection of the silyl ether (MeOH/*p*-TsOH, room temperature, 3 h) and subsequent oxidation of diol **11** with pyridinium dichromate (PDC)[13] (DMF, 40 °C, 48 h) followed by methylation with CH_2N_2 gave the diester **12**[8,14] [70% yield from **10**, oil, $[\alpha]^{25}_D$ −7.0° (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) 1740, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.66 (d, *J* = 4 Hz, 2′-H), 3.75 (s, 2 × CO_2CH_3), 1.47 and 1.40 (1:2 ratio, both s, *t*-BuO), 0.95 (d, *J* = 7 Hz, 1′-CH_3)]. Transformation of the C-4 side chain to the enal system (cf. **16**) was initiated by selective removal of the ethylene ketal group (60% AcOH, 60 °C, 24 h) to yield the aldehyde **13**[8] (oil, 64%); the C-1′ methyl group epimerized (1:1) under the reaction conditions. Introduction of the methoxy methylene group with $Ph_3P(Cl)CH_2OCH_3$/*t*-AmONa/benzene, room temperature, 30 min, followed by hydroxyselenation[15] with PhSeCl/THF/Et_3N/H_2O, room temperature, 1 h, yielded the α-selenoaldehyde **15**[8] in 90% yield.

Several trials to obtain the enal system (cf. **16** and **17**, Scheme III) under usual conditions (30% H_2O_2, $NaIO_4$, etc.) were not successful. However, oxidative removal of the selenide with O_3 (CH_2Cl_2, −78 °C), followed by trapping of the resultant benzeneseleninic acid with Et_3N afforded at 10:1 mixture of the (*E*)-enal **16**[8,16,17a] [30% yield, oil, $[\alpha]^{25}_D$ −16.4° (*c* 0.9, $CHCl_3$); IR ($CHCl_3$) 1740, 1695, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.03 (d, *J* = 8 Hz, 3′-H), 5.81 (d, *J* = 8 Hz, 2′-H), 2.14 (br s, 1′-CH_3)] and (*Z*)-enal **17**[8,16] [3% yield, oil, $[\alpha]^{25}_D$ −7.7° (*c* 0.88, $CHCl_3$); IR ($CHCl_3$) 1735, 1690, 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.85 (d, *J* = 8 Hz, 3′-H), 5.94 (dd, *J* = 1.5, 8 Hz, 2′-H), 1.86 (d, *J* = 1.5 Hz, 1′-CH_3); 50% of starting material **15** was also recovered. On the other hand, removal of the selenide of **15** by bromination (2.2 equiv of NBS/THF, room temperature, 2 min; aqueous NaOAc, 15 min) gave the (*Z*)-enal **17** as the major product (**16**:**17** = 1:2, 67% yield).[17b] The Wittig reagents **18** and **19** for the C-4 side chain were obtained by the treatment of (*R*)- and (*S*)-3-*tert*-butoxy-2-methyl-1-bromopropane,[18] respectively, with Ph_3P/toluene, 110 °C, 24 h. **18**:[8] 65% yield; mp 180–181 °C; $[\alpha]^{25}_D$ −0.4° (*c* 1.0, MeOH) **19**:[8] 65% yield; mp 180–181 °C; $[\alpha]^{25}_D$ +0.4° (*c* 1.0, MeOH).[19] Condensation of both isomers with the (*E*)-enal **16**, 2 equiv of *n*-BuLi/THF, −78 °C (2 min) and 0 °C (10 min), gave exclusively the C-5′ (*R*)- and (*S*)-dienes, (*EER*)-**20**[8] and (*EES*)-**21**,[8] which upon oxidation (Jones reagent, 0 °C, 1 h) and esterification with CH_2N_2 provided (*EER*)-**22** and (*EES*)-**23**. Comparison of the two C-5′ epimers with the corresponding derivative of domoic acid by a two-step conversion [(i) 2-(*tert*-butoxycarbonyloxyimino)-2-phenylacetonitrile (Boc-ON)/Et_3N, and (ii) CH_2N_2] showed apparent differences by 360-MHz ^1H NMR, and this led to the revision of the structure **2** to **3** as described above.[4]

Completion of the synthesis now required condensation of the *R* side chain **18** to the (*Z*)-enal **17**. This was accomplished in the same two-step sequence mentioned above to give **25**:[8,20] 35% yield from **17**; oil; $[\alpha]^{25}_D$ −47° (*c* 1.9, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 6.27 (dd, *J* = 11.8, 15.4 Hz, 3′-H), 5.94 (d, *J* = 11.8 Hz, 2′-H), 5.67 (dd, *J* = 8.0, 15.4 Hz, 4′-H), 1.66 (br s, 1′-CH_3), 1.29 (d, *J* = 6.8 Hz, 5′-CH_3). The N- and O-protecting groups were removed in two steps: (i) 2.5% KOH, room temperature, 24 h-; (ii) CF_3CO_2H, room temperature, 15 min, in quantitative yield.

(10) Treatment of **9a** with NaOMe/MeOH led to complete isomerization to the trans-isomer **9b**, suggesting that **9a** possesses the desired C-3 and C-4 cis side chains.

(11) To the best of our knowledge, this is the first example of amide reduction in the presence of an *N*-urethane protecting group on the same nitrogen atom. Treatment of the silyl ether **6** under the same reaction conditions provided *N*-*tert*-butoxycarbonyl-2-(*tert*-butyldimethylsilyl)oxymethyl pyrrolidine in 70% yield. Employment of *N*-benzyloxycarbonyl derivative of **6** was also effective and gave the N-(benzyloxy)carbonyl-2-(*tert*-butyldimethylsilyl)oxymethyl pyrrolidine in 80% yield.

(12) Brown, H. C.; Choi, Y. M. *Synthesis* **1981**, 439.

(13) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399.

(14) No lactone or acetal formation was detected. This procedure also demonstrates the effectiveness to convert N-protected α-amino alcohols into α-amino acid derivatives.

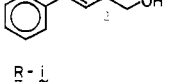
(15) Toshimitsu, A.; Aoai, T.; Owada, H.; Uemura, S.; Okano, M. *J. Chem. Soc., Chem. Commun.* **1980**, 412.

(16) Configuration of trisubstituted double bond was determined by a NOE study (an 18% NOE was observed between the C-1′ methyl group and the C-3′H for (*E*)-enal **16**, and a 14.5% NOE was observed between the C-1′ methyl group and the C-2′H for (*Z*)-enal **17**).

(17) (a) Although starting **15** is a mixture of four diastereomeric isomers, it is conceivable that the selenoxide group at C-2′ is readily isomerized in the presence of Et_3N to the thermodynamically stable conformation before syn elimination and gives rise to the (*E*)-enal **16** as the major product (employment of NaOAc instead of Et_3N afforded a 1:1.5 mixture of **16**:**17** in low yield). (b) Removal of phenyl selenide by bromination or chlorination has been reported: Masuyama, Y.; Ueno, Y.; Okawara, M. *Chem. Lett.* **1977**, 835.

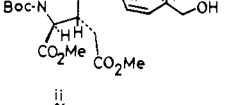
(18) (a) Cohen, N.; Eichel, W. F.; Lopresti, R. J.; Neukom, C.; Saucy, G. *J. Org. Chem.* **1976**, *41*, 3505. We thank Dr. Cohen, Hoffmann-LaRoche Inc., for a generous gift of (*S*)-(+)-3-hydroxy-2-methylpropanoic acid. (b) The *tert*-butyl group was cleaved upon heating with Ph_3P.

(19) The optical purity of the Wittig reagents **18** and **19** were ascertained by conversion into (*R*)-i ($[\alpha]^{25}_D$ +46.8° (*c* 0.75, $CHCl_3$)) and (*S*)-i ($[\alpha]^{25}_D$ −47° (*c* 0.8, $CHCl_3$) [2 equiv of *n*-BuLi/THF, −78 °C; benzaldehyde, −78 °C (2 min) and 0 °C (10 min); 65–75% yield; oil] and subsequent ^1H NMR studies with tris[3-[(trifluoromethyl)hydroxymethylene)]-*d*-camphorato]europium(III), [Eu(tfc)$_3$].



R-i
S-i, 2-epimer

(20) Wittig reaction (**17** + **18**) gave rise to the desired (*ZER*)-**24** (60%) accompanied by the (*ZZR*)-isomer ii: 15% yield, oil; ^1H NMR ($CDCl_3$) δ 6.27 (d, *J* = 11.8 Hz, 2′-H), 6.17 (t, *J* = 11.8 Hz, 3′-H), 5.15 (t, *J* = 11.8 Hz, 4′-H), 1.70 (br s, 1′-CH_3), 0.97 (d, *J* = 6.5 Hz, 5′-CH_3). Both **24** and **ii** were easily separated by medium-pressure chromatography (SiO_2; elution with a 1% MeOH–$CHCl_3$ system).



ii

The resultant trifluoroacetate (mp 125–128 °C) was treated with 1 equiv of NaOH, followed by Amberlite CG-50 (H^+ form, elution with H_2O) to give **3**[21] as white crystals; mp 213 °C (dec) (lit. mp 217 °C, dec);[3b] $[\alpha]^{25}_D$ −111° (*c* 0.2, H_2O) (lit. $[\alpha]^{25}_D$ −109.7°).[3b] Synthetic **3** was identical in all respects (paper chromatography and IR, 360 MHz ^1H NMR, ^{13}C NMR) with natural domoic acid (**3**).

Acknowledgment. We thank Professor Koji Nakanishi, Director, for discussions. We are grateful to Professor Tsunematsu Takemoto and Dr. Kyosuke Nomoto for a generous gift of natural domoic acid and discussions during the initial stage of this study.

Registry No. 3, 14277-97-5; **4**, 53100-44-0; **5**, 81658-25-5; **6**, 81658-26-6; **7**, 81658-27-7; **8**, 81671-20-7; **9a**, 81658-29-9; **9b**, 81802-29-1; **10**, 81802-30-4; **11**, 81658-31-3; **12**, 81658-32-4; **13**, isomer 1, 81802-31-5; **13**, isomer 2, 81658-33-5; **15**, 81658-35-7; **16**, 81658-45-9; **17**, 81658-36-8; **18**, 81658-46-0; **19**, 81658-47-1; **20**, 81658-39-1; **21**, 81703-61-9; **22**, 81658-40-4; **23**, 81703-62-0; **24**, 81703-63-1; **25**, 81658-41-5; (*R*)-i, 81802-32-6; (*S*)-i, 81802-33-7; ii, 81845-33-2; *trans*-2-(trimethylsilyl)-oxy-1,3-pentadiene, 81802-34-8; 2-methyl-2-ethyl-1,3-dioxolane, 126-39-6; (*R*)-3-*tert*-butoxy-2-methyl-1-bromopropane, 60782-65-2; (*S*)-3-*tert*-butoxy-2-methyl-1-bromopropane, 59965-13-8.

(21) Domoic acid (**3**): ^1H NMR (360 MHz, D_2O) δ 6.35 (dd, *J* = 11.0, 14.9 Hz, 3′-H), 6.13 (d, *J* = 11.0 Hz, 2′-H), 5.78 (dd, *J* = 7.9, 14.9 Hz, 4′-H), 3.98 (d, *J* = 8.1 Hz, 2-H), 3.83 (q, *J* = 7.6 Hz, 4-H), 3.70 (dd, *J* = 7.6, 12.3 Hz, 5α-H or 5β-H), 3.49 (dd, *J* = 7.6, 12.3 Hz, 5β-H or 5α-H), 3.29 (dq, *J* = 7.0, 7.9 Hz, 5′-H), 3.05 (dddd, *J* = 5.8, 7.6, 8.1, 9.1 Hz, 3-H), 2.75 (dd, *J* = 5.8, 16.8 Hz, 3-CH_2CO$_2$H), 2.50 (dd, *J* = 9.1, 16.8 Hz, 3-CH_2CO$_2$H), 1.81 (s, 1′-CH_3), 1.27 (d, *J* = 7.0 Hz, 5′-CH_3).

Calculated Triplet State Energies of Carbonylheme Complexes: Relevance to Photodissociation and Postulated Paramagnetic Component

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Received November 5, 1981

The possibility of low-lying paramagnetic states in iron–ligand complexes in ferrous hemoglobins, advanced by recent magnetic susceptibility measurements of Cerdonio and co-workers,[1-4] has attracted considerable attention.[5-11] In spite of an early controversy[5-7] due to the long-held view of its diamagnetic state,[12] the existence of a paramagnetic component in oxyhemoglobin[1] (HbO_2) has now been substantiated not only by the room-temperature measurements of magnetic susceptibility[2] but also by the interpretation of the temperature dependence of Mössbauer quadrupole splitting data[8] and of single-crystal Mössbauer studies.[11] Consistently, theoretical studies of an oxyheme complex[10] also predict a low-lying triplet excited state that can be in thermal equilibrium with the singlet ground state. On the other hand, the most recent report of paramagnetism in carp (carbon monoxy)-hemoglobin[3] (HbCO) is more equivocal, in view of the observed diamagnetic state of frozen human HbCO[1,12] and the small quadrupole splitting in Mössbauer resonance spectra,[13,14] both consistent with the calculated isotropic charge distribution in a singlet ferrous (t_{2g}^6, $S = 0$) state.[15] It is, therefore, important to investigate the low-energy triplet states of HbCO in order to determine whether a thermally populated paramagnetic state can be accommodated as has been suggested.[3,4]

Characterization of the triplet states of HbCO is equally important to address the unresolved questions with regard to the role of the triplet states in the process of CO photodissociation. Very recently, Stanford and Hoffman[16] have used triplet sensitization experiments to show that triplet excitation transfer to state(s) of higher than singlet multiplicity in carbonylferroporphyrin gives rise to CO dissociation. They have established an upper limit of 14 300 cm^{-1} for the energies of these states and have argued that dissociation might occur directly from the $\pi \rightarrow \pi^*$ configurations.[17] In recent studies,[18,19] however, we have shown that the singlet $d_\pi \rightarrow d_{z^2}{}^*$ states rather than $\pi \rightarrow \pi^*$ states are photodissociating and that the intersystem crossing to low-energy triplet states is not necessary for initiating dissociation but may occur as one of the early events of the photodissociation process.

In this communication, we report the results of calculations of the energy and nature of the low-energy triplet states of model carbonylheme complexes consisting of a hexacoordinated ferrous–porphyrin system with CO and imidazole axial ligands for four different iron–ligand geometries: one linear ($\alpha = 0°$, $\beta = 180°$) as in model compounds[20,21] and three nonlinear, tilted ($\alpha = 14°$, $\beta = 180°$), bent ($\alpha = 0°$, $\beta = 135°$), and kinked ($\alpha = 7°$, $\beta = 162°$) representing intact hemoproteins,[22-27] where α is the angle C–Fe–heme normal and β is the Fe–C–O bond angle. The three nonlinear geometries chosen are consistent with the known position of the oxygen atom from neutron and X-ray diffraction studies and reflect the uncertainty in the carbon atom position in intact hemoproteins. The details of the complete geometries including those of porphyrin and imidazole ligand are given elsewhere.[15] The linear geometry calculations were also repeated with the iron–imidazole system 0.24 Å from the center of the porphyrin plane with and without a corresponding displacement of CO ligand. The calculations were carried out by using an INDO-SCF-MO-LCAO-CI program[28-32] using an INDO/1 ap-

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