

**Table I.** Stereoselection of Cycloadditions of C-5 Substituted Cyclopentadienes


entry	compd	X	reaction time <sup>a</sup>	addition ratio	
				anti	syn
a	1	SH	3 h	4.5 <sup>b</sup>	5.5 <sup>b</sup>
b	2	SMe	27.5 h	9	1
c	2	SMe	46 h	11.5 <sup>b</sup>	1 <sup>b</sup>
d	3	SOMe	48 h	10	0
e	4	SO <sub>2</sub> Me	9 days	10	0
f	5	OH	<30 s	0	10
g	6	OMe	<10 min	0	10
h	7	NHAc	3.5 h	0	10
i	7	NHAc	3.5 h	trace	10 <sup>b</sup>
j	8	NH <sub>2</sub>	3.5 h	0	10 <sup>b</sup>
k	9	H	<30 s	2 <sup>13</sup>	8 <sup>13</sup>

<sup>a</sup> Approximate time for diene disappearance (TLC); reactions were run at 22 °C; yields in all cases were >90%; ratios were determined by integration of <sup>1</sup>H NMR spectra of the total reaction mixture. <sup>b</sup> *N*-phenylmaleimide adduct.

initio calculations<sup>25</sup> suggest that the electron density is decreased on the diene syn face and that the sulfur lone pair electrons interact more strongly with the diene (HOMO) than in the case of oxygen. This interaction must be disrupted prior to cycloaddition and favors the anti approach. The relative rates and stereoselection are also influenced by substituent orientation. The distal oxygen conformer is the most reactive and leads rapidly to adduct compared to the sulfur series in which both conformers have comparable energy. These factors—lone-pair interactions, conformational reactivity, and substituent electronegativity enhance anti cycloaddition in the sulfur series.

In conclusion, this study adds to our understanding of the facial preferences of addends in [4 + 2] cycloadditions of cyclopentadienes. Heteroatom-directed control of  $\pi$ -facial selectivity by variation of the substituent or through the judicious choice of mixed acetals (oxathiolane ketals) has considerable potential for the total synthesis of natural products. Approaches to multicyclic systems that utilize these features are under investigation.

**Acknowledgment.** We are grateful to Memorial University of Newfoundland and the Natural Sciences and Engineering Research Council of Canada for financial support of this research, to B. Gregory for high resolution mass spectra, to C. Jablonski for NOE and NMR measurements, to A. W. Hanson and M. J. Newlands for X-ray analysis, to R. W. Franck, P. G. McDougal, N. H. Werstiuk, R. A. Poirier, and D. J. Burnell for fruitful discussions, and to the referees for their constructive comments.

**Supplementary Material Available:** Synthetic schemes and brief reaction conditions for preparation of the dienes and adduct interconversions (2 pages). Ordering information is given on any current masthead page.

(23) Professor Franck has kindly informed us that acetylene dicarboxylates, tetracyanoethylene, and *N*-phenyltriazolinedione exhibit reversed facial selectivity in his acyclic dienes as also observed in an amino case by Kozikowski and co-workers<sup>3</sup> (also: Franck, R. W.; Tripathy, R.; Onan, K. D. *J. Am. Chem. Soc.* 1987, in press and ref 16). Thus the thiomethyl diene 2 was treated with tetracyanoethylene. A single anti adduct was obtained whose structure was established by X-ray analysis. It seems likely that in acyclic cases more reactive dienophiles afford predominantly the anti (to the oxygen and nitrogen substituent) product as a consequence of the preferential trapping of a different rotamer ratio compared to maleic anhydride. This should allow a level of facial control by variation of the dienophile. In addition, recent evidence has indicated that cyanoethylene and triazolinediones react by an aziridinium imide (1,4-zwitterion) mechanism.<sup>24</sup>

(24) Jensen, F.; Foote, C. S. *J. Am. Chem. Soc.* 1987, 109, 6376.

(25) Research in progress with N. H. Werstiuk (McMaster University) and A. Yadav and R. A. Poirier (Memorial University).

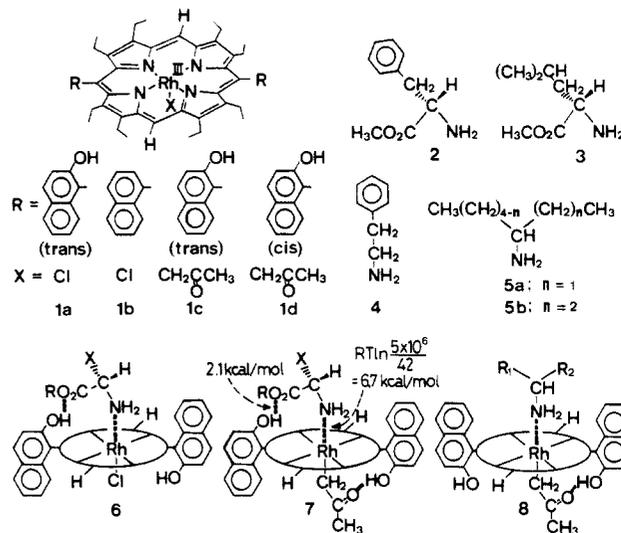
## Molecular Recognition of Amino Acids: Two-Point Fixation of Amino Acids with Bifunctional Metalloporphyrin Receptors<sup>1</sup>

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Received December 24, 1987

Amino acids can be solubilized in organic solvents in the form of ammonium or carboxylate ion upon formation of crown complexes<sup>2</sup> or hydrophobic salts.<sup>3</sup> The complexation of zwitterionic forms is generally weak,<sup>4</sup> but some elaborate receptor systems for these have been reported.<sup>5,6</sup> Nonionic amino acids (H<sub>2</sub>NCHRCO<sub>2</sub>H), on the other hand, seem to be a potential form in apolar organic solutions but have been receiving surprisingly little attention.<sup>7</sup> We report here the first successful two-point fixation of amino acids and amino esters in *nonionic forms* via simultaneous metal-coordination and hydrogen-bonding interactions with bifunctional metalloporphyrin receptors.



Chlororhodium(III) complexes of *trans*-5,15-bis(2-hydroxy-1-naphthyl)- (1a) and 5,15-bis(1-naphthyl)octaethylporphyrin (1b)<sup>8</sup> form stable 1:1 rhodium-amine adducts, in a practically irreversible manner,<sup>9</sup> with L-phenylalanine methyl ester (2) and L-leucine methyl ester (3) as well as 2-phenylethylamine (4) and 3- (5a) or 4-aminoheptane (5b) as references in CHCl<sub>3</sub>.<sup>10</sup> The

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(2) (a) Helgeson, R. C.; Timko, J. M.; Moreau, P.; Peacock, S. C.; Mayer, J. M.; Cram, D. J. *J. Am. Chem. Soc.* 1974, 96, 6762. (b) Newcomb, M.; Helgeson, R. C.; Cram, D. J. *Ibid.* 1974, 96, 7367. (c) Newcomb, M.; Toner, J. L.; Helgeson, R. C.; Cram, D. J. *Ibid.* 1979, 101, 4941.

(3) Behr, J.-P.; Lehn, J.-M. *J. Am. Chem. Soc.* 1973, 95, 6108.

(4) (a) Pedersen, C. J. *J. Am. Chem. Soc.* 1967, 89, 7017. (b) Behr, J.-P.; Lehn, J.-M.; Vierling, P. *Helv. Chim. Acta* 1982, 65, 1853.

(5) Sunamoto, J.; Iwamoto, K.; Mohri, Y.; Kominato, T. *J. Am. Chem. Soc.* 1982, 104, 5502.

(6) (a) Rebeck, J., Jr.; Nemeth, D. *J. Am. Chem. Soc.* 1985, 107, 6738. (b) Rebeck, J., Jr.; Askew, B.; Nemeth, D.; Parris, K. *Ibid.* 1987, 109, 2432.

(7) For the nature of amino acids in DMSO, see: Hughes, D. L.; Bergan, J. J.; Grabowski, E. J. *J. Org. Chem.* 1986, 51, 2579.

(8) Aoyama, Y.; Yamagishi, A.; Tanaka, Y.; Toi, H.; Ogoshi, H. *J. Am. Chem. Soc.* 1987, 109, 4735.

(9) All the adducts can be isolated by chromatography. Addition of a large excess amount of the second amine to a CHCl<sub>3</sub> solution of a preformed amine adduct led to no amine exchange. Amine adduct 1a-2 underwent no decomplexation when its CHCl<sub>3</sub> solution was stirred with 6 N aqueous HCl for 24 h.

(10) For the amine coordination to Rh(III) porphyrin, see: (a) Kadish, K. M.; Yao, C.-L.; Anderson, J. E.; Coccolios, P. *Inorg. Chem.* 1985, 24, 4515. (b) Anderson, J. E.; Yao, C.-L.; Kadish, K. M. *J. Am. Chem. Soc.* 1987, 109, 1106.

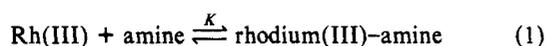
**Table I.** Binding Constants of Amines with Rhodium(III) Porphyrins in CHCl<sub>3</sub> at 15 °C<sup>a</sup>

amine	<i>K</i> (M <sup>-1</sup> ) Rh porphyrin	
	1c	1d
3	5 × 10 <sup>6</sup>	1.6 × 10 <sup>5</sup>
5b	2.9 × 10 <sup>5</sup>	3.9 × 10 <sup>5</sup>

<sup>a</sup> [Rh porphyrin]<sub>total</sub> = 4.30 × 10<sup>-5</sup> M.

<sup>1</sup>H NMR and IR spectra of adduct 1a-2 for CDCl<sub>3</sub> or CHCl<sub>3</sub> solutions showed nonequivalent OH proton resonances at δ 8.85 (1 H) and 6.00 (1 H) and ν<sub>OH</sub> and ν<sub>CO</sub> at 3430 and 1728 cm<sup>-1</sup>, respectively. A large (~3 ppm) downfield shift of one OH proton and significant shifts to lower wavenumbers in ν<sub>OH</sub> (~100 cm<sup>-1</sup>) and ν<sub>CO</sub> (14 cm<sup>-1</sup>) as compared with those for reference compounds<sup>11</sup> indicate that the adducts of 1a and amino esters contain an intramolecular hydrogen bond between OH and CO<sub>2</sub>CH<sub>3</sub> groups in addition to a common Rh-NH<sub>2</sub>- coordination bond (refer to 6, R = CH<sub>3</sub> and X = CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub> or CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>).<sup>12</sup> A similar dual interaction has been observed for the C-bound acetone-rhodium derivatives of *trans*-bis(hydroxynaphthyl)-porphyrin (1c) and its *cis* isomer (1d).<sup>8</sup> Compound 1a in CDCl<sub>3</sub> was also found to extract 1 mol of free amino acids such as phenylalanine and leucine in water at neutral pH to form similar two-point amino acid adducts (6, R = H and X = CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub> or CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>) irreversibly; ν<sub>OH</sub> centered at 3400 cm<sup>-1</sup> and ν<sub>CO</sub> 1717 cm<sup>-1</sup> for the phenylalanine adduct.<sup>13</sup>

Reversible amine coordination (eq 1) was achieved by using related Rh(III) porphyrins having an organic trans ligand in place of Cl. Amines 2-5 reversibly bind with 1c and 1d. In the latter



the acetone moiety is attached to Rh at the OH-containing side of the porphyrin plane.<sup>8</sup> The binding constants (*K*) for 3 and 5b were determined by spectrophotometric titration with good isosbestic behaviors<sup>14</sup> and are summarized in Table I. Although 1d whose open coordination site has no nearby OH groups (refer to 8) shows a slight preference for 5b over 3 (*K*<sub>1d</sub>(3)/*K*<sub>1d</sub>(5b) = 0.41), 1c binds 3 17 times more strongly than 5b (*K*<sub>1c</sub>(3)/*K*<sub>1c</sub>(5b) = 17). Although, in a different viewpoint, 5b is bound with 1d slightly more tightly than with 1c (*K*<sub>1c</sub>(5b)/*K*<sub>1d</sub>(5b) = 0.74), 3 prefers 1c to 1d by a factor of 31 (*K*<sub>1c</sub>(3)/*K*<sub>1d</sub>(3) = 31). These results indicate that the hydrogen bonding in the adduct 1c-3<sup>15</sup> (7, R = CH<sub>3</sub> and X = CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>) gives rise to a selectivity factor of 17/0.41 = 31/0.74 = 42, corresponding to a stabilization energy of *RT* ln 42 = 2.1 kcal/mol (15 °C). Reversible and highly selective amino ester binding with 1c was directly shown by the NMR spectrum for a 1:2:2 mixture of 1c, 3, and 5b in CDCl<sub>3</sub> ([1c] = 4.1 mM) affording two adducts 1c-3 and 1c-5b in a ratio of approximately 20:1.<sup>16</sup> Reversible amino acid extraction from

neutral aqueous solutions was also achieved with 1c but practically not with 1d which lacks appropriate hydroxyl groups to assist ligand binding. Thus, vigorous stirring of a CDCl<sub>3</sub> solution of 1c (4.1 mM) and a saturated aqueous solution of phenylalanine gave adduct 7 (R = H and X = CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>)<sup>17</sup> (ν<sub>CO</sub> for the CO<sub>2</sub>H group at 1720 cm<sup>-1</sup>)<sup>13</sup> together with unbound 1c in a ratio of 1:2.4. Other amino acids such as tryptophan, leucine, and isoleucine were extracted similarly. Competitive extraction of phenylalanine and leucine demonstrated no significant difference in their extractabilities, indicating that π stacking interactions<sup>6</sup> between an aromatic amino acid and the porphyrin plane are not important.

This work presents a novel example of two-point fixation of amino acids and amino esters in nonionic forms. It is significant that the weaker interaction, hydrogen bonding, in fact brings about a sizable selectivity for amino esters in homogeneous solutions and also plays a crucial role in amino acid extraction from neutral aqueous solutions. Suitable modification of the present porphyrin may allow three-point interactions<sup>18</sup> with amino acids. Tri-functional chiral metalloporphyrins have been prepared,<sup>19</sup> and further work is now under way along this line.

**Acknowledgment.** This work was supported by Grant-in-Aid from the Ministry of Education, Science, and Culture of Japan.

(16) Adducts 1c-3 and 1c-5b gave sharp NMR resonances in high field region at -30 °C: δ -5.26 and -5.60 (diastereotopic CH<sub>3</sub>COCH<sub>2</sub>-Rh), -4.69 and -5.50 (NH<sub>2</sub>), -3.10 (CHNH<sub>2</sub>), -2.10 (CH<sub>3</sub>COCH<sub>2</sub>-Rh), -1.23 (CH<sub>2</sub>C-H(CH<sub>3</sub>)<sub>2</sub>), -0.71 (CH(CH<sub>3</sub>)<sub>2</sub>), and -0.14 and -0.91 (CH(CH<sub>3</sub>)<sub>2</sub>) for 1c-3; δ -5.74 (NH<sub>2</sub>), -5.32 (CH<sub>3</sub>COCH<sub>2</sub>-Rh), -3.88 (CHNH<sub>2</sub>), -2.10 (CH<sub>3</sub>CO-CH<sub>2</sub>-Rh), and -2.60, -1.40, -1.15, -0.96, and -0.10 (CH<sub>2</sub> and CH<sub>3</sub> in amine ligand) for 1c-5b. The selectivity (1c-3)/(1c-5b) is based on integration of these high field signals in the spectrum for a 1:2:2 mixture of 1c, 3, and 5b at -30 °C.

(17) Adduct 7 (R = H and X = CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>) in the presence of unbound 1c gave sharp and characteristic NMR signals at -30 °C for the phenylalanine and acetone ligands and meso protons in a similar manner as adduct 1c-3 (7),<sup>16</sup> but both hydroxyl (in the naphthol moiety) and carboxyl proton resonances could not be detected. This was also the case for adduct 6 (R = H and X = CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>). It seems that the protons in the OH and CO<sub>2</sub>H groups which are hydrogen bonded undergo extensive broadening due to rapid exchange.

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## The C=C Double Bond of Tetrafluoroethylene

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Tetrafluoroethylene is an unusual olefin, with one of the weakest carbon-carbon double bonds known [*D*(C=C) ~ 60 kcal/mol]. Unfortunately, the experimental C=C bond energy for C<sub>2</sub>F<sub>4</sub> remains quite uncertain, with values ranging from 53 to 76 kcal/mol.<sup>1-3</sup> In addition, the nature of the double bond in C<sub>2</sub>F<sub>4</sub> has also been disputed: the importance of bent or "banana" bonds versus the conventional σ and π bonds has not been addressed quantitatively, although a recent paper has suggested that bent

(11) The corresponding absorptions for reference compounds are as follows: δ<sub>OH</sub>, 6.15 (1 H) and 5.68 (1 H) for adduct 1a-4 and 5.23 (2 H) for the free base porphyrin of 1a; ν<sub>OH</sub>, 3529 cm<sup>-1</sup> for 1a-4, 3524 cm<sup>-1</sup> for 1a, and 3520 cm<sup>-1</sup> for the free base porphyrin of 1a; ν<sub>CO</sub>, 1742 cm<sup>-1</sup> for 1b-2.

(12) Other characteristic NMR signals for 1a-2 are as follows: δ -4.42 and -5.23 (both 1 H, m, diastereotopic NH<sub>2</sub>), -3.20 (1 H, m, CHNH<sub>2</sub>), 0.07 and 0.48 (both 1 H, m, diastereotopic CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), and 10.28 and 10.20 (both 1 H, s, meso-H).

(13) A shift to lower wavenumber by ~20 cm<sup>-1</sup> in ν<sub>CO</sub> as compared with ν<sub>CO</sub> at 1737 cm<sup>-1</sup> for adduct 1b-phenylalanine is consistent with an intramolecular hydrogen bonding between OH and CO<sub>2</sub>H groups in 6 (R = H) and 7 (R = H).

(14) Compounds 1c and 1d undergo a considerable red-shift of their Soret absorption upon complex formation with amines; e.g., λ<sub>max</sub> for 1c-3 (7, R = CH<sub>3</sub> and X = CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>) (CHCl<sub>3</sub> solution) 421, 537, and 567 nm. Spectra in the region of 500-600 nm with varying amounts of amine were recorded, where isosbestic points were observed at 528, 548, and 566 nm in the case of titration of 1c with 3. Binding constants (*K*) were calculated from absorbance changes at 557 nm, a λ<sub>max</sub> for 1c, according to *K* = [rhodium-amine]/[Rh][amine].

(15) Adduct 1c-3 (7) and 1d-3 (refer to 8) showed ν<sub>CO</sub> for CO<sub>2</sub>CH<sub>3</sub> groups respectively at 1728 and 1740 cm<sup>-1</sup>, indicating a characteristic shift by 12 cm<sup>-1</sup> in ν<sub>CO</sub> for 1c-3 due to hydrogen bonding.

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(1) An indirect determination of *D*(F<sub>2</sub>C=CF<sub>2</sub>) from the heat of formation of C<sub>2</sub>F<sub>4</sub> (Δ*H*<sub>f,298</sub> = -157.4 ± 0.7 kcal/mol) and a 1977 experimental value for Δ*H*<sub>f,298</sub>(CF<sub>2</sub>) = -52 kcal/mol (Lias, S. G.; Liebman, J. F.; Levin, R. D. *J. Phys. Chem. Ref. Data* 1984, 13, 695) yields *D*<sub>298</sub> = 53.4 ± 0.7 kcal/mol.

(2) Using another (more recent) determination of Δ*H*<sub>f,298</sub>(CF<sub>2</sub>) = -44.2 ± 1 kcal/mol (Berman, D.; Bomse, D. S.; Beauchamp, J. L. *Int. J. Mass Spec. Ion Phys.* 1981, 39, 263) yields *D*<sub>298</sub> = 69.0 ± 2.7 kcal/mol.

(3) This value constitutes the only directly determined bond energy (*D*<sub>298</sub> = 76.3 ± 3 kcal/mol) for C<sub>2</sub>F<sub>4</sub> in a Knudsen cell equilibrium study at high temperature (~1200 K) by Zmbov et al. (Zmbov, K. F.; Uy, O. M.; Margrave, J. L. *J. Am. Chem. Soc.* 1968, 90, 5090).