In the DBY reduction of alkyl β-keto-α-methylbutanoates, it was reported that octyl ester showed the highest diastereoselectivity of 95 : 5 *syn* predominance.[6a] However, as noted in Table 1, the RBY, DBY, and IMBY reduction of **1** showed the reverse diastereoselectivity of 2 : 98 *anti* predominance [compound **2d**, with 40% enantiomeric excess of (2R, 3R)-**2d**[13]]. Compounds **2a** and **2c** were also found to be reduced with high stereoselectivity but the reduction ratio was relatively poor and **2f-2h** were not reduced by IMBY.

It was deduced that the one extra methylene unit of alkyl β-keto-α-methylpentanoates as compared with the corresponding butanoates caused the reversal of diastereoselectivity from *syn* to *anti* predominance. And the increased bulkiness of the pentanoates made butyl ester **1d** the most favorable substrate in terms of diastereoselectivity and reduction ratio while in case of butanoates the octyl ester was reported to be the best.[6a]

References

1. (a) S. Masamune, W. Choy, F. A. J. Kerdesky, and B. Imperiali, *J. Am. Chem. Soc.*, **103**, 1566 (1981); (b) P. A. Barlett, *Tetrahedron*, **36**, 3 (1980).
2. T. Oishi, and T. Nakata, *Acc. Chem. Res.*, **17**, 338 (1984).
3. G. Fráter, U. Muller, and W. Günzer, *Tetrahedron*, **40**, 1269 (1984).
4. (a) S. Servi, *Synthesis*, 1 (1990); (b) R. Csuk, B. I. Glänzer, *Chem. Rev.*, **91**, 49 (1991).
5. D. Buisson, C. Sanner, M. Larcheveque, and R Azerad, *Tetrahedron Lett.*, **28**, 3939 (1987).
6. (a) K. Nakamura, T. Miyai, K. Nozaki, K. Ushio, S. Oka, and A. Ohno, *Tetrahedron Lett.*, **27**, 3155 (1986); (b) K. Nakamura, T. Miyai, A. Nagar, S. Oka, and A. Ohno, *Bull. Chem. Soc. Jpn.*, **62**, 1179 (1989).
7. T. Suga, H. Hamada, and T. Hirata, *Chem. Lett.*, 471 (1988).
8. Alkyl β-keto-α-methylpentanoate (**1**) was prepared by self-condensation and transesterification. Esters of methyl (**1a**), ethyl (**1b**), propyl (**1c**), and butyl (**1d**) β-keto-α-methylpentanoate were prepared (63-80% yield) from the corresponding propionate by self-condensation (NaH). Pentyl to octyl β-keto-α-methylpentanoate (**1e-h**) were obtained by transesterification of **1b** and corresponding alcohols under acid catalysis with yield of 60-80%.
9. C. H. Heathcock, M. C. Pirrung, and J. E. Sohn, *J. Org. Chem.*, **44**, 4294 (1979).
10. H. O. House, D. S. Crumrine, A. Y. Teranishi, and H. D. Olmstead, *J. Am. Chem. Soc.*, **95**, 3310 (1973).
11. The ^{13}C-NMR and ^{1}H-NMR data of **3b** and **2b** are described as representive examples. **2b** (major): ^{13}C-NMR δ 74.8 (carbinol), 45.2 (methine), 14.3 (methyl) ppm; ^{1}H-NMR δ 3.6 (m, C-3 H), 4.0 (dp, methylene of alkoxy) ppm. **3b** (*anti*): ^{13}C-NMR δ 74.7, 45.4, 14.3 ppm; ^{1}H-NMR δ 3.6 (m), 4.0 (dq) ppm. **3b** (*syn*): ^{13}C-NMR δ 73.6, 44.8, 10.3 ppm; ^{1}H-NMR δ 3.8 (m), 4.0 (dq) ppm.
12. The GLC conditions: HP-1, 25 m×0.2 mmI.D.×0.11 μm, N_2 0.55 ml/min, injector 280℃, FID 300℃, split 30 : 1, 60℃ (2 min), to 280℃ (5℃/min).
13. To determine the absolute configuration and enantiomeric excess of **2d**, 5-hydroxy-4-methyl-3-heptanone was synthesized form **2d**. The enantiomeric excess of the **2d** was determined by measuring the optical rotation of 5-hydroxy-4-methyl-3-heptanone and the subsequent GLC (DB1701, capillary column) analysis of the corresponding MTPA ester.

Fourier Transform Raman Spectroscopic Investigation of Silver ion-Flavin Mononucleotide Complexation

Nam-Soo Lee

Department of Chemistry, Chung-buk National University, Cheong-ju 360-763

Received June 19, 1991

The excitation using near-infrared laser, CW Nd : YAG 1064 nm has been of great interest recently for photolabile and highly fluorescent compounds in Fourier transform Raman spectroscopy.[1] Resonance Raman, surface enhanced Raman, coherent Raman and infrared spectroscopy have been applied to study fluorescent free flavins and flavoproteins.[2] Metal ion bound flavins, such Ag(I) and Ru(II), were studied by resonance Raman spectroscopy as possible models for metal-flavin interactions in biological environments.[3] These metal ions are known to form 1 : 1 complex with flavin chromophores.[3b] Resonance Raman spectroscopic studies of free flavins, flavins embedded in flavoproteins, and metal ion bound flavins bear rather limited molecular informations partly because of the resonance phenomena of exciting light source with flavin chromophores. However, near-infrared laser excitation far from absorption region generates well-defined vibrational Raman spectra under non-resonant conditions.[4] The photodecomposition of sample compounds sensitive to visible light can be almost avoided using near-infrared light source. These conditions have been applied to free flavins and adsorbed flavins on the silver metal surface sucessfully.[1b]

Metal ion interactions with flavin chromophores have been extensively investigated for the electron transfer mechanism of flavoproteins through various redox and ionization states of flavins. Ag^+ ion compelx with flavins show a new band at 530 nm in the electronic absorption spectrum. The structure of 1 : 1 Ag^+-flavin complex was proposed that Ag^+ ion binds through coordinations at N_5 and the carbonyl oxygen of $C_4=O$ to form the inner sphere complex.[3b] The secondary binding site at N_1 and the carbonyl oxygen of $C_2=O$ was implied through X-ray structure study.[5]

In this paper we report Fourier transform Raman spectra by CW 1064 nm excitation of flavin mononucleotide (FMN) (Figure 1a), and 1 : 1 Ag^+-FMN complex (Figure 1b) in each powder form. FT-Raman spectrum of FMN is quite similar to that of riboflavin[1b] except the stretching region of $C_2=O$ and $C_4=O$ in flavin ring III. In that of FMN there are a broad band at 1655 cm^{-1} and a band at 1704 cm^{-1} due to carbonyl stretching modes. Lumiflavin are well studied th-

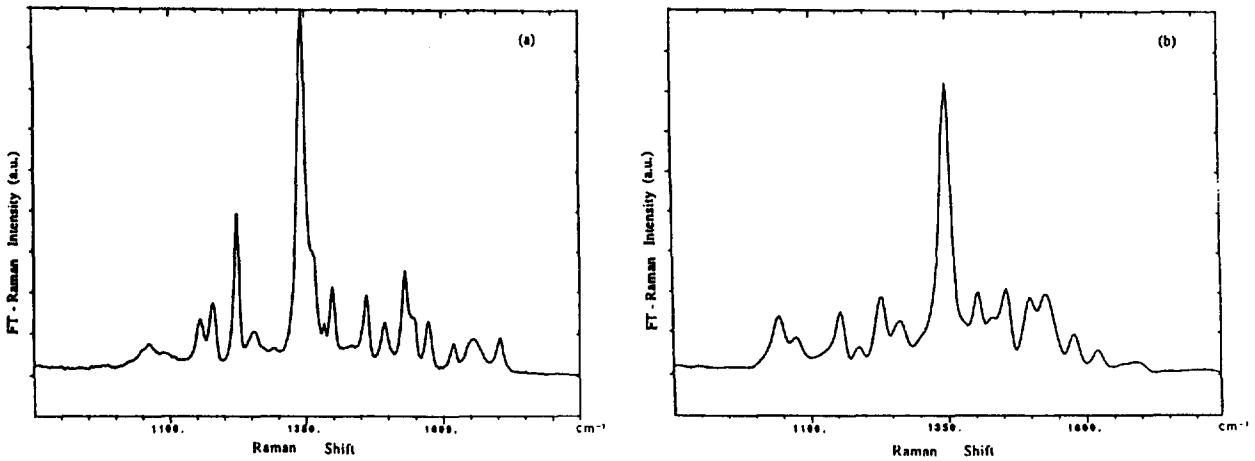


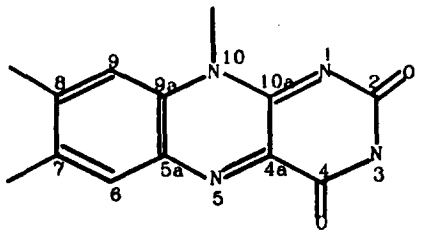
Figure 1. (a) FT-Raman spectrum of Flavin mononucleotide (FMN) in powder form. conditions: laser power=0.1 W; spectral resolution=4.0 cm^{-1}; coadding 1000 times. (b) FT-Raman spectrum of Ag^+-FMN complex in powder form. conditions: laser power=0.1 W; spectral resolution=4.0 cm^{-1}; coadding 5000 times. Each sample was dried in vacuum, and contained in ordinary melting point capillary. Both FT-Raman spectra were obtained by Bomem DA3.002 spectrophotometer equipped with liquid N_2 cooled InGaAs detector, CW 1064 nm excitation source from Quantronix Nd : YAG laser, and back-scattering collection optics system.

Table 1. Observed FT-Raman Frequencies (cm^{-1}) of Lumiflavin (LF), FMN and Ag^+-FMN, Calculated Frequencies of LF (LF[c]) and Shifts of FMN upon Complexation

No.[a]	LF[b]	LF[c]	FMN	Ag^+-FMN	Shifts	Assignments (major contributions)[a]
4	1716	1716	1704	1688	−16	stret (C_4=O), stret (C_2=O)
5	1660	1660	1655	1667	+12	stret (C_2=O), stret (C_4=O)
7	1620	1620	1620	1621	+ 1	stret ($C_{5a}C_{9a}$), stret ($C_{4a}N_5$)
8	1581	1586	1574	1579	+ 5	stret (N_1C_{10a}), stret ($N_{10}C_{10a}$)
9	1549	1548	1547	sh*		stret (N_1C_{10a}), stret ($C_{4a}N_5$)
	1537		1532	1528	− 4	
10	1513	1500	1495	1500	+ 5	stret ($C_{4a}N_5$), stret ($C_{9a}N_{10}$)
11	1463	1483	1462	1457	− 5	stret (C_7C_8), stret (C_8-Me)
13	1412	1415	1399	1405	+ 6	bend (N_3-H), stret (C_4=O)
14	1394	1386	1384	no*		stret (C_2N_3), stret (C_2N_1)
	1360		1364	sh*		
15	1345	1352	1344	1350	+ 6	stret ($C_{5a}C_6$), stret ($N_{10}C_{10a}$)
17	1283	1291	1292	1304	+12	stret ($C_{4a}C_{10a}$), stret (C_4N_3)
	1261		1255	1265	+10	
18	1234	1241	1224	1231	+ 7	stret (C_4N_3), stret (C_4C_{4a})
20	1166	1165	1180	1190	+10	stret (C_4C_{4a}), stret ($C_{4a}C_{10a}$)
21	1140	1130	1157	1156	− 1	bend (C_6-H), stret (C_7-Me)
22	1078	1101	1062	1043	−19	bend (C_9-H), bend (C_6-H)

[a]From reference 6b. [b]Observed FT-Raman frequencies in reference 1b. [c]Normal coordinate analysis in reference 6b. * sh: shoulder, no: not observed.

Flavin Ring Numbering System



rough normal coordinate analysis in the region of 2000-1000 cm^{-1} because of its structural simplicity by several different laboratories.[6] There are, however, several discrepancies in the band assignments among these normal mode calculations. Particularly the calculation by Abe and Kyogoku[6b] shows excellent similarity to the observed FT-Raman spectrum of lumiflavin.[1b] FT-Raman spectrum of lumiflavin has the common characteristics with that of riboflavin or FMN in position and intensity of each band. Therefore the bands assignments of Abe and Kyogoku for lumiflavin are applied to interpret most bands in the region of 2000-1000 cm^{-1} of FT-Raman spectrum of FMN at this moment. FT-Raman frequencies of FMN and Ag^+-FMN complex are listed in Table 1. They

are compared with the observed FT-Raman frequencies[1b] and with the normal coordinate calculation[6b] of lumiflavin by Abe and Kyogoku with their numbering system and bands assignments. The frequency shifts of FMN upon Ag^+ ion complexation are also included in Table 1. The bands which were not appeared in the normal coordinate analysis are listed without numbering.

On taking look at the Raman frequency shifts of FMN upon complexation, one can notice that vibrational modes attributed to the contribution from flavin ring I are downshiftd, but those from flavin ring II and/or III are upshifted consistantly. Only one exception is the stretching mode of $C_4=O$, the band no. 4, in flavin ring III which is downshifted as much as -16 cm^{-1}. Therefore one can propose that the coordination of metal ion at N_5 and the oxygen of $C_4=O$ induces the reduction of the ring conjugation of flavin ring II and III contributed mainly by two carbony groups of flavin ring III. This reduction of ring conjugation is responsible for the upshift of vibrational modes of flavin ring II and III and the downshift of carbonyl stretching band of $C_4=O$ as shown in FT-Raman frequencies of Ag^+-FMN complex. It implies that the carbonyl oxygen of $C_4=O$ is strongly coordinated to metal ion. The other carbonyl stretching band, the band no. 5, of $C_2=O$ is $+12$ cm^{-1} upshifted. This proposes that this site may not be responsible for the coordination of metal ion binding.

Acknowledgement. I greatly thank Prof. I. Hanazaki of Institute for Molecular Science, Okazaki, Japan for allowing me to use FT-Raman facility. This work was supported in part by Non Directed Research Fund, Korea Research Foundation and in part by Korea Science and Engineering Foundation.

References

1. (a) S. Nie, L. G. Marzilli, and N.-T. Yu, *J. Am. Chem. Soc.*, **111**, 9256 (1989); (b) H.-S. Yoo, N.-S. Lee, and I. Hanazaki, submitted for publication; (c) T. Herschfeld and B. Chase, *Appl. Spectrosc.*, **40**, 133 (1986); (d) A. Crookell, P. J. Hendra, H. M. Mould, and A. J. Turner, *J. Raman Spectroscopy*, **21**, 85 (1990); (e) J. Goral, and V. Zichy, *Spectrochimica Acta*, **46A**, 253 (1990); (f) D. L. Atkins, J. W. Macklin, and H.-R. Zhu, *J. Phys. Chem.*, **95**, 793 (1991).
2. (a) T. Kitagawa, Y. Nishina, K. Shiga, H. Watari, Y. Matsumura, and T. Yamano, *J. Am. Chem. Soc.*, **101**, 3376 (1979); (b) J. Schmit, P. Coudron, A. W. Thopson, K. L. Watters, and J. T. McFarland, *Biochemistry*, **22**, 76 (1983); (c) M. D. Morris and R. Bienstock, *Spectroscopy of Biological Systems*, R. J. H. Clark and R. E. Hester, eds., Wiley, Chichester, Vol. 13, pp. 395-442, (1986); (d) J. T. McFarland, *Resonance Raman Spectra of Polyenes and Aromatics*, T. G. Spiro, ed., Wiley, New York, Vol. 2, pp 211-302 (1987); (e) N.-S. Lee, R.-S. Sheng, M. D. Morris, and L. M. Schopfer, *J. Am. Chem. Soc.*, **108**, 6179 (1986); (f) M. Abe, Y. Kyogoku, T. Kitagawa, K. Kawano, N. Ohishi, A. Takai-Suzuki, and K. Yagi, *Spectrochimica Acta*, **42A**, No. 9, 1059 (1986).
3. (a) M. J. Benecky, M. G. Dowling, M. J. Clarke, and T. G. Spiro, *Inorg. Chem.*, **23**, 865, (1984); (b) M. J. Benecky, T.-J. Yu, K. L. Watters, and J. T. McFarland, *Biochim. Biophys. Acta*, **626**, 197 (1980).
4. M. Fujiwara, H. Hamaguchi, and M. Tasumi, *Appl. Spectrosc.*, **40**, 137 (1986).
5. C. J. Fritchie, Jr., *J. Biol. Chem.*, **23**, 7459 (1972).
6. (a) C. R. Lively and J. T. McFarland, *J. Phys. Chem.* **94**, 3980 (1991); (b) M. Abe and Y. Kyogoku, *Spectrochim. Acta*, **43A**, 1027 (1987); (c) W. D. Bowman and T. G. Spiro, *Biochemistry*, **20**, 3313 (1981).