Tetrahedron Letters,Vol.30,No.17,pp 2257-2258,1989
Printed in Great Britain

0040-4039/89 $3.00 + .00
Pergamon Press plc

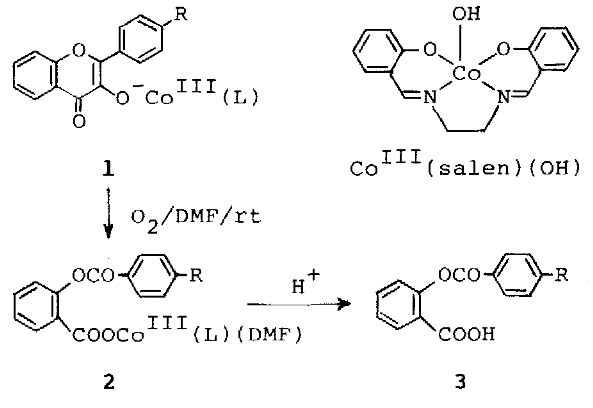
SUBSTRATE ANION COBALT(III) COMPLEX INTERMEDIATE IN MODEL QUERCETINASE REACTION USING COBALT SCHIFF BASE COMPLEX

Akira NISHINAGA,* Naoki NUMADA, and Kazushige MARUYAMA
Department of Applied Chemistry, Osaka Institute of Technology
Ohmiya 5, Asahi-ku, Osaka 535, Japan

Summary: 4'-Methoxyflavonolatocobalt(III)(salen), a key intermediate for model quercetinase reaction is synthesized. The complex undergoes dioxygenolysis of the heterocyclic ring in DMF by apparently a nonradical process.

Cobalt Schiff base complexes [Co(SB)] mimic reactivities of some dioxygenases including quercetinase:[1] e.g. Co(salen) [salen = N,N'-ethylenebis(salicylideneiminato)] catalyzes in DMF dioxygenolysis of the heterocyclic ring in flavonols to give the corresponding depside and carbon monoxide.[2] Substrate anion cobalt(III) complexes have been commonly posturated as the reactive intermediates for all model dioxygenase reactions using Co(SB).[1] However, no direct evidence for such substrate anion complex intermediate has been obtained. We wish to report here synthesis and characterization of a flavonolatocobalt(III) complex (**1**) as the intermediate for the model quercetinase reaction. We find that complex **1** is quite stable against O_2 in noncoordinative solvents but undergoes dioxygenolysis in the presence of a coordinative nitrogen base, and that the dioxygenation step seems not to involve the substrate radical. The present finding provides a significant aspect for understanding the quercetinase reaction.

4'-MethoxyflavonolatoCo^{III}(salen) (**1a**) is obtained as fine crystals (87% yield) by mixing Co^{III}(salen)(OH)[3] with 4'-methoxyflavonol in CH_2Cl_2 at room temperature followed by addition of ether. The analytical data ($C_{32}H_{25}N_2O_6Co$: C, ±0.35%; H, ±0.25%; N, ±0.05%) are in good agreement with the structure **1a**. The ^{1}HNMR ($CDCl_3$) of **1a** shows sharp signals at δ 3.8 (s, 3H), 3.6-4.2 (m, 4H), 6.5-8.5 ppm (m, 18H), indicating that the complex is diamagnetic. The signals (multiplet) for the ethylene group in **1a** is characteristic for a twist conformation of the Schiff base ligand.[4] Addition of acetic acid to a solution of **1a** in CH_2Cl_2 gives the starting flavonol and Co^{III}(salen)(OAc) quantitatively, supporting the structure **1a**. Complex **1b** is similarly obtained from flavonol. When a solution of **1a** in CH_2ClCH_2Cl is allowed to stand at room temperature or refluxed even under oxygen for 3 h, **1a** is all recovered. Heating a solution of **1a** in DMF under nitrogen resulted also in no reaction. These results show that the Co-O bond of the flavonolato moiety in **1a** is unsusceptible to homolytic cleavage. Interestingly, however, when oxygen is bubbled through a solution of **1a** in DMF at room temperature, the electronic spectrum of the solution is



a; R = MeO **b**; R = H L = salen

changed with time following first order kinetics ($k = 9.5 \times 10^{-5} s^{-1}$) (Fig. 1), and the product anion cobalt(III) complex (**2a**) ($C_{34}H_{32}N_3O_8Co$: C, ±0.33%; H, ±0.30%; N, ±0.18%) is obtained quantitatively from the final solution. The 3-C atom in the substrate is released as CO.[2] Treatment of **2a** with an acid gives a depside **3a**. The dioxygenolysis of **1a** takes place also in pyridine (py). Similar reactions occur also with **1b**. These results suggest that the selective dioxygenation may be accomplished by coordinatiion of the donor base such as DMF or py to the Co^{III} center in **1** so as to enhance an O_2 sensitive anionic natur of the flavonolato moiety,[5] and that no free substrate radical is involved in the dioxygenation step: a radical chain autoxidation mechanism can be ruled out. The nonradical dioxygenation step may be rationalized by assuming a charge transfer nature for the transition state involving a substrate anion and O_2.[1,6] In the Co^{II}(salen) catalyzed oxygenolysis of 1 in DMF,[1] $[Co^{III}(salen)(DMF)]_2(O_2)$, a μ-peroxo complex formed initially,[7] reacts with the substrate to form **1** coordinating DMF. The active species in the catalytic cycle should be the product anion complex of type **2**. Actually, **2a** shows the same catalytic activity as Co^{II}(salen) does for the oxygenation of 4'-methoxyflavonol in DMF.

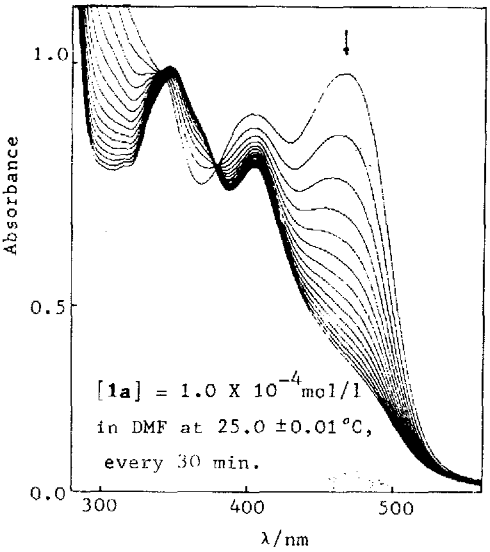


Fig. 1. Spectral change in oxygenation of **1a** in DMF.

References

1 A. Nishinaga and H. Tomita, J. Mol. Catal., 1980, **7**, 128. A. Nishinaga, Protein, Nucleic Acid and Enzyme ISSN 0371-8565, 1983, **26**, 214.
2 A. Nishinaga, T. Tojo, H. Tomita, and T. Matsuura, J. Chem. Soc. Chem. Commun., 1974, 896.
3 A. Nishinaga, T. Kondo, and T. Matsuura, Chem. Lett., 1985, 905.
4 R. J. Cozens, K. S. Murray, Aust. J. Chem., **25**, 911 (1972). The twist conformation of the salen ligand may be rationalized by assuming coordination of the flavonolato group as a bidentate ligand.
5 A. Nishinaga, T. Tojo, H. Tomita, T. Matsuura, J. Chem. Soc. Perkin Trans. I, **1979**, 2511.
6 C. W. Jefford and P. A. Cadby, Fortschritte d. Chem. org. Naturst., 1981, **40**, 191.
7 E. C. Niederhoffer, J. H. Timmson, A. E. Martell, Chem. Rev., **84**, 137 (1984).

(Received in Japan 6 March 1989)