methyldisilazane, $M'N(SiMe_3)_2$ (M' = Li, Na, K), yield bis(trimethylsilyl)amido complexes,[28] in contrast to the synthesis of silylimido complexes from the amine.

Vanadium (trimethylsilyl)imido complexes **6a,b** are formed by addition of 2 equiv of ligand to $V(NSiMe_3)Cl_3$ (**5**) and can only be prepared in solvents from which they immediately precipitate. In solution, **6a,b** rapidly lose $ClSiMe_3$, yielding the previously reported nitrido complexes $V(N)Cl_2L_2$.[6] In contrast, we find that the analogous bipyridine complex, $V(NSiMe_3)Cl_3(bpy)$, reported by Dehnicke and co-workers,[10] requires hours at ambient temperature in benzene for elimination of $ClSiMe_3$ to occur, producing the nitrido derivative, $V(N)Cl_2(bpy)$.[29] Since loss of ligand is much less favorable for chelating bipyridines, as is observed for **3c**, this suggests that generation of a vacant coordination site at the metal center may be necessary for elimination of $ClSiMe_3$ and formation of the nitrido complex.[30] Alternatively, the lower reactivity of the bpy complex may reflect its poor solubility in benzene. Due to their high reactivity, **6a,b** are characterizable only by the products of their decomposition and by IR spectroscopy. Note that, as for the niobium and tantalum compounds described above, the (trimethylsilyl)imido ligands in **6a,b** originate from hexamethyldisilazane via $NH_4VO_3 + NH(SiMe_3)_2 \rightarrow V(NSiMe_3)(OSiMe_3)_3$[5,9a] $\rightarrow V(NSiMe_3)Cl_3$[6] $\rightarrow V(NSiMe_3)Cl_3L_2$.

The fast, clean elimination of $ClSiMe_3$ from the vanadium silylimido chloro compounds **5** and **6** contrasts with the slow, incomplete reactions of the niobium and tantalum derivatives **1-4**. The reasons that compounds **1-4** do not undergo stoichiometric loss of chlorotrimethylsilane are not clear but may possibly reflect an instability of M≡N: for niobium and tantalum. To date, all reported nitrido derivatives of these two metals have bridging structures with M—N distances in the range expected for double bonds;[31] there are no examples of niobium or tantalum terminal nitrido complexes. Likewise, triply bonded terminal oxo and imido complexes of niobium and tantalum are limited in number.[32] In contrast, vanadium forms short strong triple bonds to oxo and imido ligands in a wide range of compounds[32] and vanadium nitrido derivatives possess extremely short V-N triple bonds in both terminal and bridged linear-chain structures, $[V(N)Cl_2L_2]_n$[6a] (Figure 1b). If stoichiometric loss of $ClSiMe_3$ from the niobium and tantalum silylimido chloro compounds requires, at some point, a triply bonded terminal or highly asymmetric bridging nitride, this could prevent complete condensation. Instead of formation of $M(N)Cl_2L_2$, incomplete loss of $ClSiMe_3$ yielding small oligomeric or cluster nitride derivatives without niobium- or tantalum-nitrogen triple bonds, could be preferred.

Our work to date suggests that cleavage of the N-Si bonds of silylimido ligands is a general reaction, though not always stoichiometric. It is interesting to contrast this to the lack of reactivity of the N-C bond of organoimido ligands. The only reported example of cleavage of this bond is the formation of an osmium(VI) nitrido anion, $[Os(N)Cl_5]^-$, upon reaction of $Os(N\text{-}t\text{-}Bu)(O)_3$ and HCl.[33] Thus, despite the close similarity between *tert*-butylimido and (trimethylsilyl)imido ligands, complexes containing these ligands have significantly different chemistries. The features that have made silyl substituents so useful in organic chemistry clearly can be harnessed for both the synthesis and subsequent reactions of inorganic compounds. We are continuing to explore this rich area of chemistry.

Acknowledgment. We gratefully acknowledge support of this work by the Air Force Office of Scientific Research, Air Force Systems Command, USAF, Grant No. AFOSR-87-0362, and by the donors of the Petroleum Research Fund, administered by the American Chemical Society.

(28) Harris, D. H.; Lappert, M. F. In *Organometallic Chemistry Reviews: Organosilicon Reviews*; Seyferth, D., Davies, A. G., Fischer, E. O., Normant, J. F., Reutov, O. A., Eds.; Elsevier: Amsterdam, 1976; pp 13-102. Lappert, M. F.; Power, P. P.; Sanger, A. R.; Srivastava, R. C. *Metal and Metalloid Amides*; Ellis Horwood: Chichester, U.K., 1980; Chapter 8.
(29) Scherfise, K. D.; Dehnicke, K. *Z. Anorg. Allg. Chem.* **1986**, *538*, 119-122.
(30) Preliminary mechanistic evidence indicates that this is also the case for reactions 1 and 2: Jones, C. J.; Lerchen, M. E.; Doherty, N. M. Unpublished results.
(31) Plenio, H.; Roesky, H. W.; Noltemeyer, M.; Sheldrick, G. M. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1330-1331. Hörner, M.; Frank, K.-P.; Strähle, J. *Z. Naturforsch. B: Anorg. Chem., Org. Chem.* **1986**, *41B*, 423-428. Frank, K.-P.; Strähle, J.; Weidlein, J. *Z. Naturforsch., B: Anorg. Chem., Org. Chem.* **1980**, *35B*, 300-306.
(32) Reference 22, Chapters 2 and 5.
(33) Clifford, A. F.; Kobayashi, C. S. *Inorg. Synth.* **1960**, *6*, 204-208.

Contribution from the Department of Natural Sciences, Western New Mexico University, Silver City, New Mexico 88061, and Department of Chemistry, Montana State University, Bozeman, Montana 59717

Models of Vitamin B_6 Enzymes. 3. Steric and Electronic Effects in Carbon-Hydrogen Bond Breaking Reactions of Bis(salicylideneglycinato)cobaltate(III) Anions

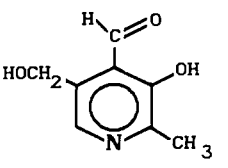
James R. Fischer,*[†] Ross J. Fischer,[†] and Edwin H. Abbott*[‡]

Received January 9, 1989

Salicylaldehydes readily form Schiff bases with glycine. These schiff bases form bis(salicylideneglycinato)cobaltate(III) complexes. Twelve cobalt(III) complexes have been synthesized with substituents variously on the 3-, 4-, 5-, and 6-positions of the aromatic ring of the salicylaldehyde moiety. The carbon-hydrogen bond breaking reactions of the two *gem*-methylenic protons of the glycine moiety have been studied by deuterium exchange. Rates are first order in complex and first order in hydroxide ion. Rates differ for the exchange of the two protons, and their ratio varies from 0.81 to 4.7. This demonstrates a reversal of stereoselectivity, depending on ring substituents. Rates vs substituents generally follow Hammett behavior. The structural and electronic features that lead to stereoselectivity are discussed.

Introduction

Stereo- and enantioselective reactions are of considerable current interest, as is the catalysis of reactions in which carbon-hydrogen bonds are broken. Vitamin B_6 model reactions offer approaches to the study of both these topics. Vitamin B_6 is, in one form, the heterocyclic aldehyde pyridoxal (I). It is an esssential cofactor



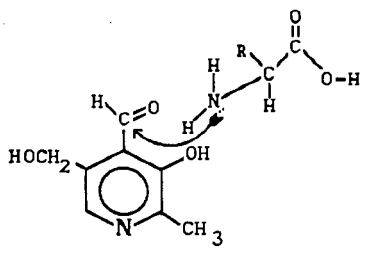
I

to many enzymes that catalyze a wide variety of reactions modifying the structure of amino acids.[1] The reactions proceed first

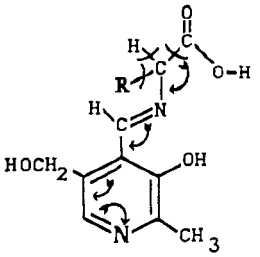
[†] Western New Mexico University.
[‡] Montana State University.

0020-1669/90/1329-1682$02.50/0

through Schiff base formation at the enzyme active site, II. The



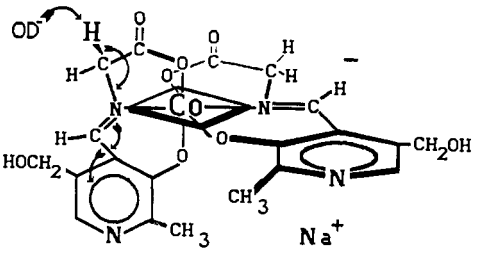
II



III

next step is often an electron shift such as that indicated by the arrows in III and resulting in the cleavage of a bond to a substituent at the amino acid α carbon atom.[1]

Dunathan has pointed out that the substituent to be cleaved can be selected by orienting its bond properly with respect to the π system of the azomethine function.[2] The closer to 90° the dihedral angle is between the bond to be cleaved and the nodal plane of the π system, the more rapid the reaction. The Dunathan hypothesis has been supported by studies of reactions of vitamin B_6 Schiff bases in solution.[3] However, since free rotation occurs around the C–N single bond, a detailed interpretation is complicated. We have prepared vitamin B_6 model compounds that permit an examination of reactivity and orientation. The compounds consist of pyridoxylidine amino acid Schiff bases coordinated to the substitutionally inert cobalt(III) ion.[4] These compounds are useful because they are sufficiently rigid that they maintain their structure during the time scales of kinetic studies of hydrogen–deuterium exchange at the amino acid α-carbon atom. In our model system, the glycyl chelate ring is not planar and the two methylene protons are held at different angles to the plane of the π system. We demonstrated differential reactivity of the geminal glycyl protons in the bis(pyridoxylideneglycinato)cobaltate(III) anion (IV) and showed that the more



IV

reactive of the two protons is in the most geometrically favorable position from the Dunathan viewpoint.[4] Additional support for this view will be published shortly.[5]

The Dunathan theory is electronic. Other workers have investigated the importance of steric effects in related systems. Bosnich et al. prepared a chiral cobalt(III) complex containing the 2-picolinoyl amide of glycine as well as a tridentate diprolyl ligand.[6] An 8-fold difference in exchange rate was observed for the glycine methylene protons. Golding and Sargeson et al. and Golding et al. studied cobalt(III) complexes in which glycine was present as a bidentate *N*-arylamine and two ethylenediamine ligands were present.[7,8] A 4-fold difference in rate was observed for one of their three compounds. All three groups of workers support mechanisms whereby hydroxide ion removes a proton from the glycine methylene group to form a planar carbanion, which is subsequently reprotonated by water. Steric factors impede the removal of one proton with respect to the other and favor reprotonation from one side of the carbanion chelate ring rather than the other. Bosnich has pointed out that these two processes are equivalent because of the principle of microscopic reversibility.[6] These three studies involve molecules with considerable steric congestion. Nonetheless, Golding et al. have pointed out that considering steric factors alone may be an "oversimplification".[8]

In our view, electronic factors are more likely to be important in cases where conjugation is extended through the glycine nitrogen atom upon deprotonation whereas steric factors are more likely to dominate when bulky groups are substituted close to the exchanging protons, for example on the nitrogen atom. In the present study, we sought to vary the steric and electronic features of an extensive series of closely related complexes also containing glycine schiff bases. 2-Hydroxypyridinecarboxaldehydes present synthetic difficulties, and so a salicylaldehyde series was chosen. Ikawa and Snell had demonstrated that 4- or 6-nitrosalicyldehyde—but not other salicylaldehydes—could catalyze some of the same sort of amino acid reactions as does pyridoxal.[9] Burrows and Bailar had synthesized the salts of the bis(salicylideneglycinato)cobaltate(III) anion.[10] The hydrogen–deuterium exchange kinetics of this compound and its 3-methyl homologue were studied by Belokon et al. as models for vitamin B_6.[11-14] Ando and Emoto have shown that the relationship of rate and substituent of a B_6 type racemization catalyzed by substituted salicylaldehydes follows the Hammett equation.[15] However, the system they studied involved Cu(II) and an excess of amino acid in dynamic equilibrium. Since the speciation was not investigated, it is not possible to determine the intrinsic reactivity of the Schiff base complexes from their data.

Experimental Section

Salicylaldehyde Syntheses. The following salicylaldehydes were obtained from the suppliers noted, checked for purity by NMR, and used without further purification. The mnemonic abbreviations for each resulting glycyl–Co(III) complex is shown in parentheses. From Aldrich: Salicylaldehyde (Sal); 3-methoxysalicylaldehyde (3-MeO); 4,6-dimethyoxysalicylaldehyde (4,6-diMeO); 3-ethoxysalicylaldehyde (3-EtO); 5-bromosalicylaldehyde (5-Br); 3,5-dibromosalicylaldehyde (3,5-diBr); 2-hydroxy-1-naphthaldehyde (Nap). From Kodak: 5-nitrosalicylaldehyde (5-Nit). 3-Methylsalicylaldehyde (3-Me) was prepared from 2-cresol by orthoformylation, variously, by the Reimer–Tiemann reaction,[16] the Duff reaction,[17] and the method of Casiraghi[18] et al. The last was the most convenient. 5-Methylsalicylaldehyde (5-Me) was prepared from 4-cresol by the method of Casiraghi et al. 3-Isopropyl-6-methylsalicylaldehyde (Thym) and 3-*tert*-butylsalicylaldehyde (3-*t*-Bu) were prepared by the Duff reaction from, respectively, thymol and 3-*tert*-butylphenol (Aldrich). 4-Nitrosalicylaldehyde (4-Nit) was prepared from 2-methyl-5-nitroaniline (Aldrich) by the sequence of diazotization to the phenol, acetylation to 4-nitro-2-acetoxytoluene,[19] and chromic acid oxidation to 4-nitro-2-acetoxybenzal diacetate with subsequent hydrolysis[20]

(1) (a) Metzler, D. E.; Ikawa, M.; Snell, E. E. *J. Am. Chem. Soc.* **1954**, *76*, 648–652. (b) Martell, A. E. *Adv. Enzymol. Relat. Areas Mol. Biol.* **1982**, *53*, 163–199.
(2) Dunathan, H. C. *Proc. Nat. Acd. Sci. U.S.A.* **1966**, 712–716.
(3) Tsai, M.-D.; Weintraub, H. J. R.; Byrn, S. R.; Chang, C.-J.; Floss, H. G. *Biochemistry* **1978**, *17*, 3177.
(4) Fischer, J. R.; Abbott, E. H. *J. Am. Chem. Soc.* **1979**, *101*, 2781–2782.
(5) Sykes, A. G.; Larsen, R. D.; Fischer, J. R.; Abbott, E. H. Manuscript in preparation.
(6) Dokuzovic, Z.; Roberts, N. K.; Sawyer, J. F.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1986**, *108*, 2034–2039.
(7) Golding, B. T.; Gainsford, G. T.; Aerlt, A. J.; Sargeson, A. M. *Tetrahedron* **1976**, *32*, 389–397.
(8) Golding, B. T.; Ioannou, P. V.; Sellers, P. J. *Inorg. Chim. Acta* **1981**, *56*, 95–98.
(9) Ikawa, M.; Snell, E. E. *J. Am. Chem. Soc.* **1954**, *76*, 653–655.
(10) Burrows, R. C.; Bailar, J. C., Jr. *J. Am. Chem. Soc.* **1966**, *88*, 4150–4156.
(11) Belokon, Y. N.; Belikov, V. M.; Vitt, S. V.; Savel'eva, T. F.; Burbelo, V. M.; Bakhmutov, V. I.; Aleksandrov, G. G.; Struchkov, Y. T. *Tetrahedron* **1977**, *33*, 2551–2564.
(12) Belokon, Y. N.; Melikyan, A. S.; Salel'eva, T. F.; Bakhmutov, V. I.; Vitt, S. V.; Belikov, V. M. *Tetrahedron* **1980**, *36*, 2327–2335. See also refs 13 and 14.
(13) Belokon, Y. N.; Melikyan, A. S.; Bakhmutov, V. I.; Vitt, S. V.; Belikov, V. M. *Inorg. Chim. Acta* **1981**, *55*, 117–124.
(14) Belokon, Y. N.; Sagiyan, A. S.; Ponomarenko, I. V.; Bakhmutov, V. I.; Belikov, V. M. *J. Chem. Soc., Perkin Trans. 2* **1985**, 21–27.
(15) Ando, M.; Emoto, S. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 2366–2368 and references cited therein.
(16) Kemp, D. S. *J. Org. Chem.* **1971**, *36*, 202–204.
(17) Duff, J. C. *J. Chem. Soc.* **1941**, 547–550.
(18) Casiraghi, G.; Casnati, G.; Puglia, G.; Sartori, G.; Terenghi, G. *J. Chem. Soc. Perkin Trans. 1* **1980**, 1862–1865.
(19) Segessar, J. R.; Calvin, M. *J. Am. Chem. Soc.* **1942**, *64*, 825–826.
(20) Bavin, E. M.; Rees, R. J. W., Robson, J. M., Seiler, M.; Seymor, D. E.; Suddaby, D. *J. Pharm. Pharmacol.* **1950**, *2*, 764–772.

Table I. Analytical Data for Sodium Bis(X-salicylideneglycinato)cobaltate(III) Compounds

compd	% C		% H		% N	
	calcd	found	calcd	found	calcd	found
5-Me, $Na[Co(5\text{-}MeSal:gly)_2]\cdot 1.5H_2O$	48.89	48.68	4.31	4.31	5.70	5.68
3-MeO, $Na[Co(3\text{-}MeOSal:gly)_2]\cdot 1.5H_2O$	45.90	46.12	4.04	4.06	5.35	5.36
4-MeO, $Na[Co(4\text{-}MeOSal:gly)_2]\cdot H_2O$	46.70	46.36	3.91	4.40	5.45	5.41
5-MeO, $Na[Co(5\text{-}MeOSal:gly)_2]\cdot H_2O$	46.70	46.64	3.91	4.45	5.45	5.39
4,6-diMeO, $Na[Co(4,6\text{-}diMeOSal:gly)_2]\cdot 2H_2O$	44.61	44.60	4.42	4.39	4.72	4.62
3-EtO, $Na[Co(3\text{-}EtOSal:gly)_2]\cdot 2.5H_2O$	46.40	46.55	4.78	4.97	4.91	5.00
4-Nit, $Na[Co(4\text{-}nitroSal:gly)_2]\cdot 2.5H_2O$	37.84	37.90	3.00	2.98	9.81	9.68
5-Nit, $Na[Co(5\text{-}nitroSal:gly)_2]\cdot 2H_2O$	38.45	38.00	2.87	2.84	9.96	9.89
5-Br, $Na[Co(5\text{-}BrSal:gly)_2]\cdot 1.5H_2O$	34.81	34.63	2.43	2.75	4.51	5.03
3,5-diBr, $Na[Co(3,5\text{-}diBrSal:gly)_2]\cdot H_2O$	28.08	28.18	1.57	1.92	3.64	3.60
Thym (3-isopropyl-6-methylSal), $Na[Co(Thym:gly)_2]\cdot H_2O$	55.12	55.12	5.69	5.97	4.94	4.74
Naphth (2-hydroxy-1-naphthaldehyde), $Na[Co(Naphth:gly)_2]\cdot 1.5H_2O$	55.43	55.12	3.76	5.97	4.97	4.28
3-*t*-Bu, $Na[Co(3\text{-}t\text{-}BuSal:gly)_2]\cdot 2H_2O$	53.43	53.99	5.86	5.94	4.79	4.74

Table II. NMR Chemical Shifts (Chemical Shifts vs TMS in ppm, Multiplicity,[a] *J*(s) in Hz)

compd	azo-methine	ring protons				glycyl AB		methyl	methoxyl	other
		H-6	H-5	H-4	H-3	downfield	upfield			
Sal	8.52 s	7.48, d-d, 1.6, 7.8	6.68, t, 7.4	7.06, t-d, 1.6, 7.8	6.60, d, 8.4	5.03, 19.7	4.94			
3-Me	8.43, s	7.28, d, 7.5	6.59, t, 7.4	6.86, d, 6.9		4.97, 19.6	4.88	1.35, s		
5-Me	8.43	7.26, d, 1.8	...	6.89, d-d, 2.1, 8.7	6.48, d, 8.6	4.99, 20.3	4.90	2.11, s		
3-MeO	8.43	7.09, d-d, 1.3, 7.8	6.58, t, 7.8	...	...	5.02, 20.1	4.91		3.25	
4-MeO	8.38	7.38, d, 8.7	6.30, d-d, 2.3, 8.7	...	6.08, d, 2.2	4.96, 19.8	4.89		3.55	
5-MeO	8.43	7.03 d, 3.2	...	6.72, d-d, 3.2, 9.1	6.47, d, 9.1	4.98, 20.2	4.90		3.68	
4,6-diMeO	8.75	...	5.83, d, 2.1	...	5.74, d, 1.9	4.96, 19.8	4.89		3.79	3.54 MeO
3-EtO	8.48	7.16, d-d, 1.6, 7.9	6.54, t, 7.8	6.70, d-d, 1.6, 7.7	...	5.04, 19.6	4.95	0.86, t, 7.1 (ethoxy methyl)		3.29 and 3.11, AB of q, 7.1, 9.6 (diastereomeric ethoxy methylene)
4-Nit	8.73	7.70, d, 8.6	7.42, d-d, 2.2, 8.7	...	7.30, d, 2.1	5.12, 19.8	5.04			
5-Nit	8.73	8.52, d, 2.8	...	7.87, d-d, 2.8, 9.3	6.66, d, 9.4	5.14, 19.8	5.06			
5-Br	8.47	7.61, d, 2.6	...	7.12, d-d, 2.6, 9.0	6.48, d, 9.0	5.01, 20.2	4.95			
3,5-diBr	8.50	7.61, d, 1.8	...	7.51, d, 1.8	...	5.07, 19.5	4.93			
Thym[b]	8.80	...	6.43, d, 7.5	6.80, d, 7.5	...	5.06, 19.5	4.33	0.76, d, 6.8; 0.39, d, 6.9 (isopropyl methyls diastereomeric)		2.73, p+, 6.7 (isopropyl methine)

[a] d = doublet, d-d = doublet of doublets, t = triplet, q = quartet, and p = quintet. [b] Thym = 3-isopropyl-6-methyl.

(8% overall yield; mp 129–131 °C uncorrected, reported mp 133–134 °C). The proton NMR spectra of all salicylaldehydes were consistent with the expected structures.

Preparation of Sodium Bis(salicylideneglycinato)cobaltate(III) Complexes. The cobalt(III) hydroxide method (method B) of Burrows and Bailar was used for all syntheses of cobalt(III) complexes.[10] The solvent used for all preparations was methanol. The total solid products were recovered by removal of the methanol under reduced pressure. The products were dark brown powders, very fine crystals, or flakes. The complexes were dried in vacuo over phosphorus(V) oxide for several days. Analytical samples were submitted to Galbraith Laboratories, Knoxville, TN, for microanalysis. Approximately half the compounds were repurified by the technique described below, but this did not have a significant influence on the elemental analysis. Table I reports the analytical data for each compound. With the exception of that for 3-*t*-Bu, the NMR spectra were consistent with the expected structures. In the 3-*t*-Bu case, several unexplained peaks were observed in addition to those expected. These were apparently due to a second compound, possibly isomeric, which was not separated by subsequent purification.

Purification of the Complexes. The compounds reported here are sufficiently unstable in the solid state that repurification was necessary prior to a kinetic analysis if the compound had been stored for any length of time. After several months, it was found that solutions prepared from these solids usually contained traces of a light brown insoluble material. Also, proton resonances were often broadened slightly, perhaps due to traces of Co(II). Further purification was necessary before NMR kinetic and long-range coupling studies could be executed. Portions of the complexes (0.5–3.0 g) were dissolved in a minimum amount of water (10–200 mL depending on solubility), filtered through a 0.2-μm membrane filter, and extracted three times with 0.05 M 8-hydroxyquinoline in chloroform and then three times with chloroform. Water was removed at reduced pressure, and the solids were dried in vacuo over phosphorus(V) oxide.

NMR Studies. NMR studies were performed on a Bruker WM-250 instrument. Chemical shifts reported in this paper were all measured at 250 MHz with 2–5 mg of the complexes dissolved in 0.7-mL portions of deuterium oxide (Aldrich 99.997% D) (Nap in methanol-d_4) and referenced to an internal HMDS capillary with chemical shifts subsequently corrected to TMS values (Table II) as $\delta_{TMS} = \delta_{HMDS} + 0.13$.

Kinetic Studies. From 1 to 4 mg of a complex was dissolved in 0.7 mL of D_2O, which contained sodium bicarbonate–carbonate buffer that was 1.0 M in KCl to control ionic strength. Total buffer concentrations were 0.05, 0.10, or 0.20 M. The results reported in Table III were for solutions 0.1 M in total carbonate. At 5.4 T the glycine methylene protons appear as a well-resolved AB pattern, and it is possible to separately integrate the A and B parts accurately. Integrals were recorded over a period of 0.5–3 h directly in the NMR spectrometer at a probe temperature of 21 ± 0.1 °C. After 24 h, no resonances could be observed in the AB region. By consideration of the relative HOD and C–H concentrations, the residual C–H integral of the region would be expected to be about 1% of its initial value, which is less than instrumental accuracy. Pseudo-first-order rate constants, ψ, were determined by a least-squares plot of

Table III. Second-Order Kinetic Rate Constants for Individual Glycyl Hydrogen Exchange Reactions and Four-Bond Coupling Constants between Azomethine and Glycyl Protons

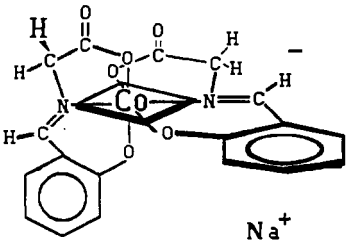
compd	second-order reaction rate consts			pD	coupling consts[a]	
	downfield	upfield	ratio (U/D)		downfield	upfield
Sal	9.0	11.7	1.3	10.27–10.67	1.74	1.76
3-Me	1.07	4.7	4.4	10.59–10.67	1.54	1.86
5-Me	6.04	9.0	1.5	10.60–10.75	1.72	1.72
3-MeO	7.9	6.4	0.81	10.22–10.41	1.62	1.84
4-MeO	1.8	2.6	1.43	10.46	1.58	1.65
5-MeO	3.94	9.18	2.5	10.53	*b*	*b*
4,6-diMeO	0.69	1.1	1.6	10.43	(1.27)	(1.37)
3-EtO	3.8	7.0	1.8	10.41	(1.27)	(1.56)
4-Nit	325	289	0.88	9.24–9.39	1.89	1.91
5-Nit	110	151	1.4	9.31	(2.8)	(2.8)
5-Br	11.0	14.0	1.3	10.46	(2.6)	(2.6)
Thym	0.16	0.66	4.3	11.19	*b*	*b*

[a] In Hz. The values shown are from Gaussian multiplied spectra with negative line broadening with valley/peak resolution of 40% or better. Couplings shown in parentheses are estimated from ordinary spectra where the peaks are less resolved (valley/peak ≥90%). [b] Not determined.

the logarithm of each integral vs time. Since the integrals at infinite time were too small to measure accurately, they were assumed to be zero for the calculation. Good first-order behavior was observed over at least the first half of the reactions. Secondary isotope effects were too small to measure reliably under these circumstances. pD's were calculated as pD = pH + 0.41. pOD was calculated as pOD = 14.869 − pD. Second-order rate constants were calculated as $k = \psi/[OD^-]$ after demonstrating that pseudo-first-order rate constants varied linearly with $[OD^-]$.

Results and Discussion

Sodium Bis(salicylideneglycinato)cobaltate(III) Complexes. These complexes were prepared by the methods published by Burrows and Bailar for the Sal compound.[10] One member of the series (Sal) has been structured by X-ray crystallography.[21] On the basis of these facts, and the analytical and NMR data reported above, the complexes are bis tridentate meridonal species as in V. The ligands are approximately planar and are at right angles



V

to one another. Such complexes are dissymmetric, and the protons of the glycine methylene group are diasteriotopic. The methylene protons appear as an AB pattern near 5.0 ppm. Each half of the AB pattern is further split by four-bond, pseudoallylic coupling to the azomethine proton. This is illustrated in Figure 1. The coupling constants to each half of the AB pattern are different from one another, indicating different dihedral angles for each methylene C–H bond with respect to the plane of the π system of the aromatic ring.[22]

Rates of Deuterium Exchange. Variation of the total carbonate–bicarbonate concentration and of pH showed that proton exchange at the glycine methylene group is a second-order reaction following the rate law in eq 1.[11] No dependence on carbonate

$$\text{rate} = k[\text{complex}][OD^-] \quad (1)$$

ion concentration could be reliably demonstrated. Table III reports the rate constants and rate ratios for the reactions we have studied.

For 10 of the compounds, the upfield wing of the AB glycyl resonance disappears more rapidly than the downfield wing. Ratios of upfield to downfield rates range from 1.3 for Sal and 5-Br to 4.4 for 3-Me. For two compounds, 3-MeO and 4-Nit, the downfield wing of the glycyl resonance disappears more

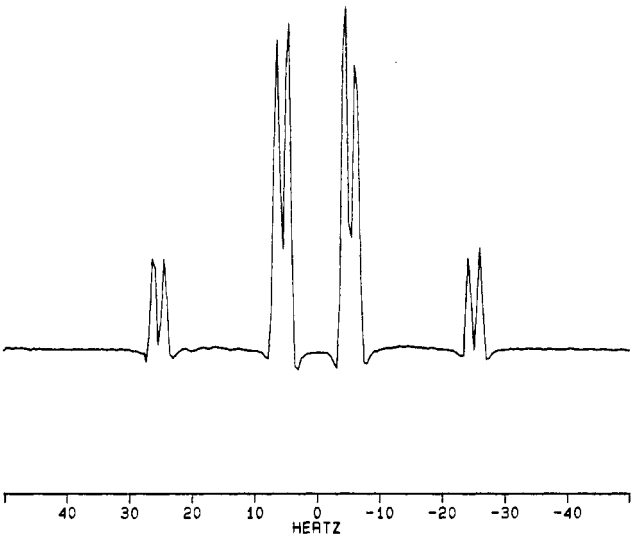


Figure 1. Proton magnetic resonance spectrum of the glycyl methylene resonance of the bis((4-nitrosalicylidene)glycinato) cobaltate(III) anion. Resolution has been enhanced by Gaussian multiplication so that the four-bond coupling of the azomethine proton is clearly visible in each wing of the AB.

rapidly, with upfield to downfield ratios of 0.81 and 0.88, respectively. On the basis of decomposition reactions and the analysis of partially deuterated glycine, Belokon assigned the more rapidly exchanging hydrogen of 3-Me to the one furthest from the aromatic ring—and the 3-methyl group—of the other ligand.[11] In accord with that assignment, we assign the upfield wings of the AB patterns to the hydrogen furthest from the aromatic ring of the other ligand in the other 11 new compounds because the chemical shift and AB coupling constants are virtually identical and there is no reason to expect that the magnetic anisotropy would be significantly different in any of the compounds.

At 250 MHz, resolution of the pattern is sufficiently good that rates could be measured for the A and B protons separately. In the cases where the rates are comparable, two separate resonances are observed for the two different geminal HD glycine compounds present at intermediate and late times. This is illustrated in Figure 2. In the cases where the upfield proton exchanges substantially more rapidly than the downfield proton, the geminal HD intermediate in which the high-field proton has exchanged first is more prominent than is the isomeric geminal HD intermediate. This is illustrated in Figure 3. In the two cases where exchange of the upfield protons is slower than that of the downfield protons, the geminal HD intermediate in which the low-field proton had exchanged first is the more prominent. These observations provide qualitative affirmation of the quantitative results we report. Golding et al. observed this type of H–D growing in their study of *N*-arylaminoglycyl complexes.[8] In the benzyl case, where they

(21) Aleksandrov, G. G.; Struchkov, Y. T.; Belokon, Y. N. *Zh. Strukt. Khim.* **1975**, *16*, 875–883.
(22) Barfield, M.; Spear, R. J.; Sternhell, S. *Chem. Rev.* **1976**, *76*, 593–624.

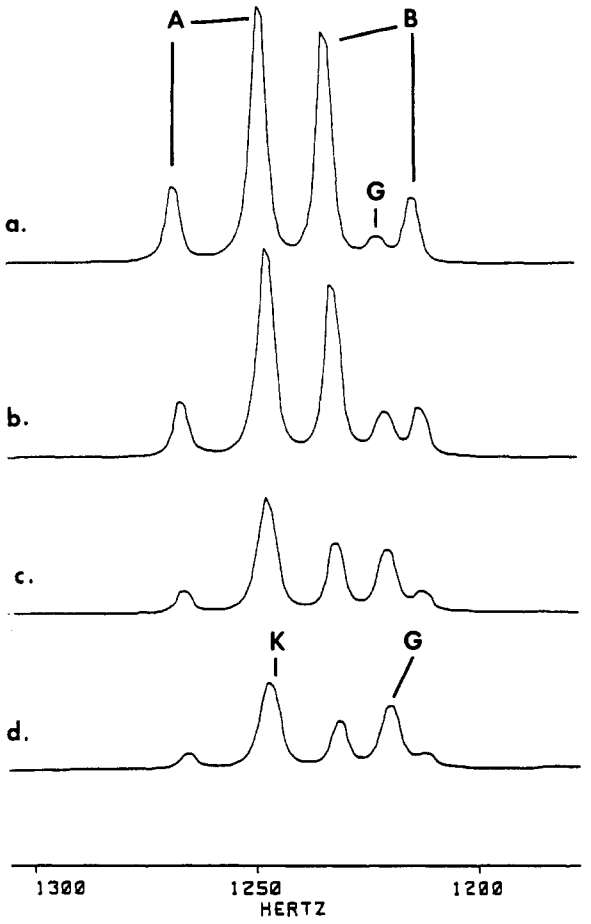


Figure 2. Proton magnetic resonance spectrum (250 MHz) of the glycyl methylene region of the bis((3-methoxysalicylidene)glycinato)cobaltate(III) anion as deuterium exchange progresses. In spectrum a, the glycyl AB pattern is marked. A new peak, G, in the upfield wing corresponds to the *gem*-HD glycyl resonance in which the downfield proton has been exchanged for deuterium. Deuterium substitution causes upfield shifts and so that other *gem*-HD glycyl resonance (K) nearly superimposes on the more intense downfield resonance of the AB. Both *gem*-HD resonances are clearly visible in the concluding phase of the reaction when they predominate.

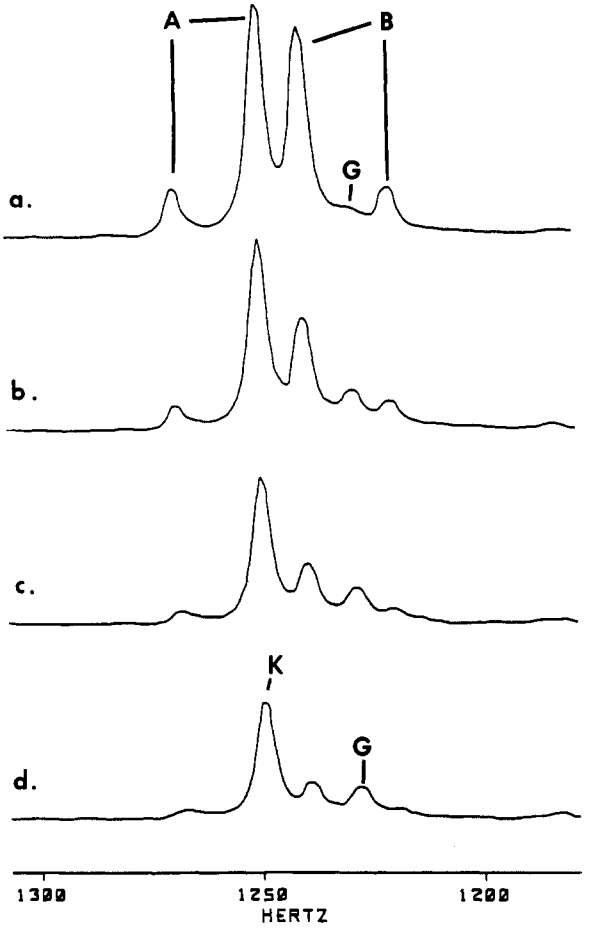


Figure 3. Proton magnetic resonance spectrum (250 MHz) of the glycyl methylene region of the bis((3-ethoxysalicylidene)glycinato)cobaltate(III) anion as deuterium exchange progresses. In spectrum a the glycyl AB is marked. A new peak, G, corresponds to the *gem*-HD glycyl resonance in which the downfield proton has been exchanged for deuterium. Resonance K corresponds to the *gem*-HD glycyl resonance in which the upfield proton has been exchanged for deuterium. Deuterium substitution causes upfield shifts, and so K nearly superimposes on the more intense downfield resonance of the AB. In the concluding phase of the reaction, K clearly predominates G, in keeping with the rate ratios reported and in contrast to Figure 2.

observed a 4-fold selectivity for the upfield proton of the glycyl AB pattern, a large intermediate CHD peak was observed between the (upfield) wings with some broadening of the inner peak of the downfield wing. Bosnich et al. did not observe a resolved AB pattern. They did observe that the CHD resonance shifted upfield but unfortunately still overlapped the CH_2 peak, requiring a more complex analysis than in our systems.[6]

Hammett Behavior of Exchange Rates. Figure 4 is a Hammett plot of the kinetic data for the compounds we have studied. The least-squares correlations line was fitted to all points except those for 3-Me and Thym. The equation of the line is $\log k = 1.43\sigma + 0.751$, with R = 0.955. The value chosen for the 4-nitro substituent was $\sigma_p = 1.27$. The σ_p^- value is appropriate for a system that generates a carbanion in conjugation with the 4-nitro substituent.[23,24] The choice of $\sigma = 0.54$ for the 4,6-dimethoxy substitution was based on twice the accepted methoxy[4,6] σ_p value of −0.27. We are not aware of a generally accepted value for methoxy σ_o. We chose to use the same value as σ_p since ortho electronic effects should be similar and, unlike many other reactions where ortho steric interference prevents development of a uniform value, the reaction center is sufficiently remote that direct steric interactions should be minimal. The value is within the range reported by other workers. In addition, it is generally

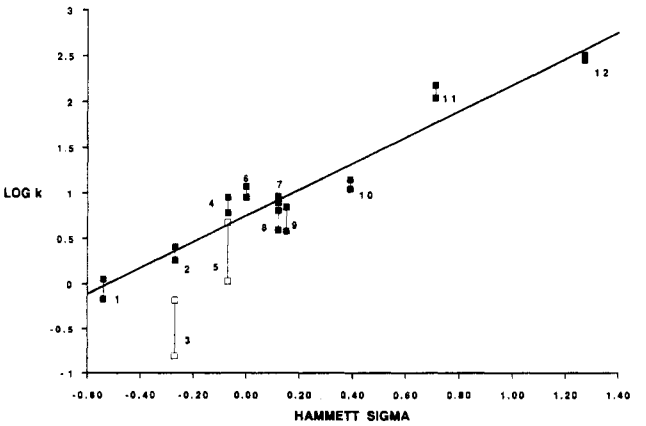


Figure 4. Hammett plot for reactions at 21 °C for the line log k = $1.433\sigma + 0.751$: 1 = 4,6-diMeO; 2 = 4-MeO; 3 = Thym; 4 = 5-Me; 5 = 3-Me; 6 = Sal; 7 = 5-MeO; 8 = 3-MeO; 9 = 3-EtO; 10 = 5-Br; 11 = 5-Nit; 12 = 4-Nit. Shaded boxes were fitted to the line; open boxes were not fitted to the line.

appropriate to sum the individual σ's for multiple substitution.[24] Exclusion of the 4,6-di-MeO value has little effect on the correlation of the line.

The value of ρ from Figure 4 is 1.43. This is considerably larger than the value reported by Ando and Emoto (0.89) for the X–

(23) Johnson, C. D. *The Hammett Equation*; Cambridge University Press: London, 1973; pp 3, 28–29, 92–93.
(24) Jaffe, H. H. *Chem. Rev.* **1953**, 53, 191–261.

salicylaldehyde; Cu(II)-catalyzed racemization of L-glutamic acid. A high value of ρ indicates a more efficient transfer of electronic effects from the substituents to the reactive center. It may be a reflection of the more rigid coordination in the systems we have studied. However, the systems studied by Ando and Emoto had a 10-fold excess of L-glutamic acid. Equilibria are complex, and speciation differences were not analyzed for the different systems. It is possible that their value of ρ reflects not only differences in reactivity but also differences in degrees of complex formations as substituents are varied.

Coupling Constants and Distortions at the Glycine Methylene CH_2. The four-bond proton-proton spin coupling between a glycine methylene proton and the azomethine proton is expected to be a function of the dihedral angle between these bonds. Table III reports those coupling constants. It is observed that the high-field methylene proton is always equally or more strongly coupled than is the low-field proton. These coupling constants can be converted into dihedral angles using $^4J_{H-H} = -2.2 \sin^2 \phi$.[5,22]

Nature of the Stereoselectivity of Proton Exchange at the Glycine Methylene Group. Two explanations may be offered for the reason the glycine methylene protons exchange at different rates. One explanation is electronic in nature and is derived from the Dunathan hypothesis described above. The proton with the greatest dihedral angle with the plane of the π system should be most acidic and exchange more rapidly. This explanation has been suggested for the pyridoxal system in which the glycine proton with the largest coupling to the azomethine proton exchanges most rapidly.[4] An alternate explanation is based on steric factors. In this explanation, steric factors impede the removal of one of the methylenic protons of the reactant and discriminate against reprotonation of the carbanion intermediate from the same side of the ligand plane. This explanation has been offered to explain the selectivity in 3-Me and other related systems.[6-8] In the 3-Me compound, presumably, it is the 3-methyl group of one ligand that impedes the reprotonation on one side of the other ligand. While we hoped that our present study would provide a clear resolution between electronic and steric effects, a review of the results show that evidence can be selected to support either model. For example, 3-Me has the greatest rate difference of any system reported herein. Figure 4 shows that, on a Hammett plot, the slowly exchanging proton rate falls far below the line, indicating, perhaps, that steric effects impede its rate and result in the observed selectivity. On the other hand, space-filling molecular models do not indicate substantial steric problems for reprotonation in aqueous media. Also, if steric factors were operating, the more bulky 3-isopropyl group of Thym, the 3-methoxy group of the 3-MeO, and the 3-ethoxy group of the 3-EtO might be expected to cause even greater selectivity than does the 3-methyl substituent; however, this is not the case. Moreover, in two of the compounds studied in this work, the selectivity in proton exchange is the reverse of the others and there is certainly no obvious steric explanation. Additional work investigating the effect of even more bulky groups in the 3-position is under way.

Chelate ring conformations vary in this series of compounds. It has been demonstrated by X-ray crystallography that the azomethine and glycyl chelate rings are planar in the Sal case[21] but puckered in the pyridoxal case.[5] Puckering results in different dihedral angles between the two glycyl methylene protons and the plane in the π system, which, according to the Dunathan hypothesis, should affect the rate of carbon-hydrogen bond breaking. This difference is revealed in the difference in four-bond coupling constants betwen the azomethine proton and each methylene proton. These coupling constants are nearly identical in the Sal case, in keeping with its observed planarity, but are very different in the 3-Me case, indicating a substantially puckered ring. In the present work, it was hoped that there would be a simple relationship between those coupling constants and the reactivity of the compounds, but this does not appear to be the case. It is possible that the conformations differ in a complicated way from compound to compound. Until structures for a representative group of substituted salicyl chelates have been determined, it will not be possible to provide a detailed assessment of the relative contributions of steric and electronic effects of stereoselectivity in these compounds. However, it appears that, whatever the role of steric factors, electronic factors are important.

Conclusions

1. The rates of glycyl carbon-hydrogen bond breaking are strongly influenced by inductive and resonance effects of substituents on the aromatic ring.
2. In this system, the inductive effects are considerably larger than had been previously reported for an analogous system.
3. For each compound, the glycyl protons exchange at different rates. The degree of stereoselectivity depends on the nature of remote ring substituents.
4. Ring substitutents cause small distortions from planarity of the azomethine and glycyl chelate rings.

Acknowledgment. The complexes studied in this paper were prepared at WNMU by Gail Stanford, Mary Kappel, Phillip Welsh, David Lambert, William VanDran, and J. Antonio Lopez as part of requirements for Chemistry 304 and 485. We also gratefully acknowledge support of this work through a Flinn Foundation—Cottrell College Science Grant C-2511 from the Research Corp. and grants from the WNMU Research Committee at Western New Mexico University and through Grant CHE 7826160 from the National Science Foundation at Montana State University.

Supplementary Material Available: A table, in spreadsheet format, containing a more detailed summary of the kinetic results (1 page). Ordering information is given on any current masthead page.

Contribution from the Department of Chemistry,
The University of North Carolina, Chapel Hill, North Carolina 27599-3290

Synthesis and Dioxygen Reactivity of Dinuclear Copper-Phenolate and Copper-Phenol Complexes with Pyrazole and Pyridine Donors

Thomas N. Sorrell*,[1] and Vivian A. Vankai

Received September 25, 1989

New hybrid ligands containing pyrazole and pyridine have been prepared; and the reaction chemistry of their copper(I) derivatives has been studied. These dinucleating ligands provide three nitrogen donors to each metal ion, and a phenol or phenolate group to bridge between the metals. The reaction of the different dicopper(I) species with dioxygen follows patterns established previously for analogous pyridyl ligands; and peroxo and hydroperoxo adducts can be generated at low temperature.

There is convincing evidence to suggest that hemocyanin contains an endogenous protein bridging ligand in at least some of its derivatives,[2] and before the crystal structure of deoxyHc had been determined,[3] a phenolate group was considered a likely

0020-1669/90/1329-1687$02.50/0