Kinetics of the Stereoselective Deuteration of Malonate Hydrogens in Some Bis(malonato)cobalt(III) Compounds and the Reversal of Stereoselectivity Induced by the Solution pH[1]

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The deuteration rates at malonate methylene groups have been measured for several $[Co(mal)_2(N)_2]^-$ ions over the pD range of 2 to 9 at 36.4 °C, where mal=malonate ion, $(N)_2$=ethylenediamine, *cis*-$(NH_3)_2$, 1,3-propanediamine, *N,N'*-dimethylethylenediamine, *cis*-$(pyridine)_2$, and 1,10-phenanthroline. The malonate deuteration is acid-catalysed at pD less than about 4 and base-catalysed at higher pD in all the compounds. In the amino-containing compounds (the first four compounds), the reaction proceeds stereoselectively in both high and low pD regions. Though the degree of the stereoselectivity depends upon the compound, the fast-exchanging hydrogen is, for all the amino-containing compounds, the one which is adjacent to the coordinating nitrogen atom. The mechanisms of acid- and base-catalysed deuteration, as well as the origin of the stereoselectivity, are discussed. For the ethylenediamine and *cis*-$(NH_3)_2$ compounds, reversal of the stereoselectivity takes place at around pD=8 and 9, respectively, and the fast-exchanging hydrogen becomes the one farthest apart from the coordinating nitrogen. Concomitant with this reversal, both malonate and amine exchange rates fall together. Thus, the rate of hydrogen-deuterium exchange at the NH_3 groups does not show the usual first-order dependence upon the OD^- concentration. These observations are explained by a mechanism in which equally reactive malonate and amine hydrogens compete for OD^- catalyst.

In the preceding paper,[2] we investigated the deuteration kinetics of malonate methylenes in monomalonatocobalt(III) compounds. The chelated and the non-chelated malonate ligands behaved quite differently and the deuteration mechanisms are discussed. The acidity of the malonate hydrogens coordinated to Co(III) has been studied by several workers. Yoneda and Morimoto[3] observed that the malonate deuteration proceeds quite easily simply by dissolving malonatocobalt(III) compounds in deuterium oxide. Buckingham *et al.*[4] noted that the malonate methylenes of $[Co(mal)_2(en)]^-$ and $[Co(mal)(en)_2]^+$ ions[5] undergo acid-catalysed and probably base-catalysed deuteration. They also found that the two types of hydrogens of coordinated malonate in $[Co(mal)_2(en)]^-$ exchange with deuterium at unequal rates. Recently, Farago and coworkers[6] made temperature dependence studies on the malonate deuteration of $[Co(mal)_2(en)]^-$, $[Co(mal)(en)_2]^+$, and $[Co(mal)(bpy)_2]^+$ in the pD region of 2 to 3. The last result confirmed that the deuteration is acid-catalysed. Here we have examined the deuteration rates of malonate ligands in $[Co(mal)_2(N)_2]^-$ type of compounds over the pD range of 2 to 9 and at 36.4 °C.

Experimental

Materials. Deuterium oxide (99.8 atom%D minimum) was obtained from E. Merck(Darmsdadt). *cis*-$K[Co(mal)_2(NH_3)_2]$[7] $2.5H_2O$, and *cis*-$K[Co(mal)_2(py)_2]3.5H_2O$[8] were prepared after Shibata *et al.* $K[Co(mal)_2(en)]H_2O$ was prepared and resolved by *levo*-$[Co(NO_2)_2(en)_2]^+$ after Dwyer and coworkers.[9] The tn complex was made after Brennan *et al.*[10] and the number of water molecules of crystallization was 2.5 instead of 2. Found: N, 6.69; C, 25.81; H, 4.38%. Calcd for $K[Co(mal)_2(tn)]\cdot 2.5H_2O$: N, 6.65; C, 25.66; H, 4.55%.

The phen compound was prepared as follows. The tris(malonato)cobalt(III) solution was prepared after Kneten and Spees[11] from 24 g(0.08M) of $Co(NO_3)_2\cdot 6H_2O$. To the filtered $[Co(mal)_3]^{3-}$ solution, 15.9 g(0.08M) of 1,10-phenanthroline monohydrate was added. After stirring at 45 °C for 1 h the solution was left standing at room temperature overnight. The precipitate, $[Co(mal)(phen)_2]$ $[Co(mal)_2(phen)]$, was filtered and redissolved in water. The double complex salt was loaded on an SP-Sephadex C-25 cation-exchange column, and eluted with water. The anionic eluent containing $[Co(mal)_2(phen)]^-$ was reloaded on a QAE-Sephadex A-25 anion-exchange column and eluted with a concentrated solution of potassium chloride. The concentrated eluent was kept in a refrigerator overnight to give needle-like crystals. Yield was about 2.0 g. Found: N, 4.84; C, 37.07; H, 2.91%. Calcd for $K[Co(mal)_2(phen)]\cdot KCl\cdot 5H_2O$: N, 4.80; C, 37.03; H, 2.59%.

Measurements. All the compounds were dissolved in deuterium oxide to about 0.20 to 0.30 mol dm^{-3}. Ionic strength was not controlled. The solution pD was adjusted by appropriate amount of HCl or K_2CO_3 and measured by a Hitachi-Horiba Model F-7 pH meter with a microelectrode accessory, immediately after kinetic measurements. The apparent pH meter readings were converted to the pD values by the empirical formula developed by Fife and Bruice,[12] pD=pH(meter readings)+0.35(at 36.4 °C). Nuclear magnetic resonance spectra were run at 36.4 °C on a Varian T-60 spectrometer operating at 60 MHz. Chemical shifts were referred to internal sodium 2,2-dimethyl-2-silapentane-5-sulfonate(DSS).

Absorption spectra were obtained on a Shimadzu UV-200 double beam spectrophotometer and circular dichroism spectra on a JASCO J-40CS spectropolarimeter.

Deuteration Rates. The hydrogen-deuterium exchange rates at amine groups were obtained from the slope of the plots of ln(intensity) *vs.* time, as in the previous studies.[13]

For malonate exchange, we first note that $[Co(mal)_2(N)_2]^-$ contains two types of malonate hydrogens, see Fig. 1. In the figure, H_N is adjacent to the coordinated nitrogen atom and H_O is close to the malonate oxygen atom. These two types of hydrogens give rise to an AB quartet immediately after dissolution of the compounds, see Fig. 2. If only H_N is deuterated, we have the species D–C–H_O, which should yield the H_O singlet. In Fig. 2, the H_O hydrogen is assumed to resonate at a higher magnetic field, in accordance with our assignment (*vide infra*). The rate constant for this process is

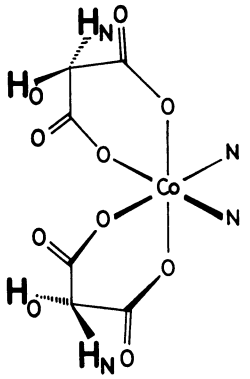


Fig. 1. A schematic presentation of the $[Co(mal)_2(N)_2]^-$ ion, showing that there are two types of malonate hydrogenes, H_N and H_O.

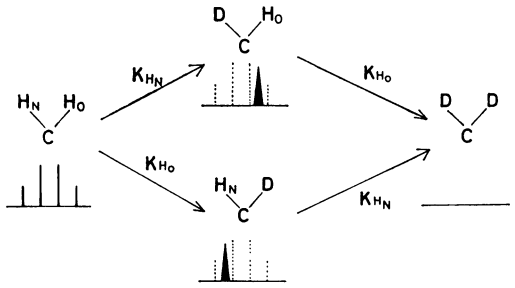


Fig. 2. The scheme for hydrogen-deuterium exchange kinetics of the H_N–C–H_O fragment. Kinetic isotope effect is not taken into account.

denoted as k_{HN}. Similarly, the species H_N–C–D produced by deuteration of only H_O would give rise to the H_N singlet. As the deuteration of H_N–C–H_O proceeds, the intensity of the initial quartet will decrease and that of the H_O and/or H_N singlet(s) will grow. This is the first stage of deuteration. Since both H_O and H_N are exchanged with deuterium in due course, these singlets diminish in intensity with time and eventually vanish. If we neglect the kinetic isotope effect[14] expected for the disappearance of H_N and H_O singlets, the rate constants for the decrease of these singlets are k_{HN} and k_{HO}, respectively. The situation is illustrated schematically in Fig. 2. We may set up simultaneous kinetic equations for the scheme of Fig. 2.

$$-\frac{d}{dt}[H_N\text{-}C\text{-}H_O] = (k_{HO}+k_{HN})[H_N\text{-}C\text{-}H_O] \quad (1)$$

$$-\frac{d}{dt}[D\text{-}C\text{-}H_O] = k_{HO}[D\text{-}C\text{-}H_O] - k_{HN}[H_N\text{-}C\text{-}H_O] \quad (2)$$

$$-\frac{d}{dt}[H_N\text{-}C\text{-}D] = k_{HN}[H_N\text{-}C\text{-}D] - k_{HO}[H_N\text{-}C\text{-}H_O], \quad (3)$$

where $[D\text{-}C\text{-}H_O]$, for example, is the concentration at time t of the species D–C–H_O and the other notations have similar meanings. Equation 1 is equivalent to

$$[H_N\text{-}C\text{-}H_O] = [H_N\text{-}C\text{-}H_O]_{t=0} \exp[-(k_{HN}+k_{HO})t]. \quad (4)$$

Namely, since H_N–C–H_O is to give either D–C–H_O or H_N–C–D or both, the rate constant for the decrease of the AB quartet, k_Q, is the sum of two rate constants k_{HN} and k_{HO},

$$k_Q = k_{HN} + k_{HO}. \quad (5)$$

Experimentally, k_Q was obtained as follows. The natural logarithms of the averaged intensity of the inner pair of the AB quartet and that of the outer pair of the quartet were plotted separately against time. These two plots gave straight lines and the slopes of these lines were the same within experimental error. The avarage of the two slopes was taken as the rate constant k_Q.

Equations 2 and 3 can be solved to give

$$[D\text{-}C\text{-}H_O] = [H_N\text{-}C\text{-}H_O]_{t=0}\{\exp(-k_{HO}t) - \exp[-(k_{HO}+k_{HN})t]\} \quad (6)$$

$$[H_N\text{-}C\text{-}D] = [H_N\text{-}C\text{-}H_O]_{t=0}\{\exp(-k_{HN}t) - \exp[-(k_{HO}+k_{HN})t]\}. \quad (7)$$

Equations 6 and 7 tell us that in the initial stage of deuteration the H_O and/or H_N singlet(s) will grow in intensity with rate constant k_{HN} and/or k_{HO}, respectively, owing to the process H_N–C–H_O→D–C–H_O and/or H_N–C–D. Experimentally, it was difficult, however, to follow these initial processes over the whole pD range simply because the rates were too large in some pD region. We are forced, therefore, to estimate the separate rate constant by following the decrease in singlet intensity, which was found to be almost exponential. This corresponds to the second stage of deuteration.

Results and Discussion

Figure 3 gives the tracings of the NMR spectra in pure deuterium oxide for all the complexes investigated here. Chemical shift data are summarized in Table 1. In Fig. 3, the strong peak at δ 4.62 is due to solvent HDO. The *cis*-$(NH_3)_2$ compound, Fig. 3(a), gives the AB quartet centered at δ 3.43 and a broad resonance at δ 3.80 due to the coordinated ammonia groups. The tn compound, Fig. 3(b), shows the complex multiplets of methylene groups at δ 2.28 (C_1 and C_3 methylenes) and δ 1.95 (C_2 methylene), and a broad absorption at δ 4.62 due to the coordinated amine group (overlapped with the HDO resonance), in addition to the malonate quartet. The spectrum of the en compound, Fig. 3(c),

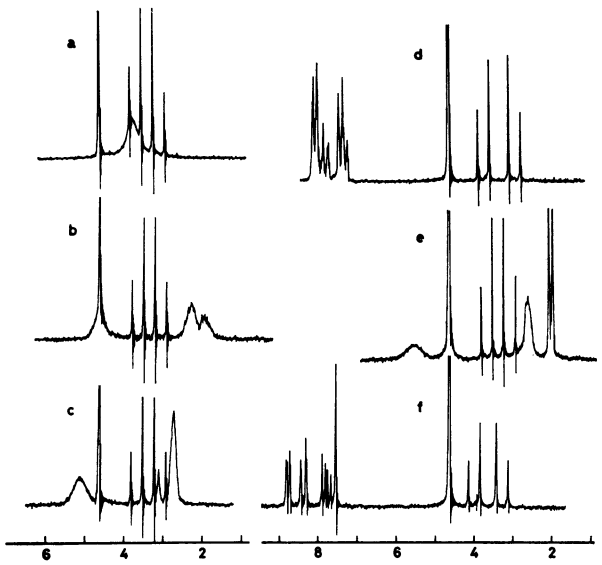


Fig. 3. The 60 MHz spectra of $[Co(mal)_2(N)_2]^-$ compounds, where $(N)_2$ stands for (a) *cis*-$(NH_3)_2$, (b) tn, (c) en, (d) *cis*-py_2, (e) dmen, and (f) phen. These spectra were taken immediately after dissolution in pure D_2O.

TABLE 1. SUMMARY OF THE CHEMICAL SHIFTS AND THE COUPLING CONSTANTS, BOTH VALUES BEING EXPRESSED IN Hz

The isotope shifts(Hz) are taken to be plus for upfield shifts in the resonance of CHD group compared with the resonance of CH_2 group, in accordance with the usual convention.

Ligand	CH_2 species		CHD species		Isotope shift		J	pD	Concn (mol dm^{-3})
	$\nu(H_N)$	$\nu(H_O)$	$\nu(H_N)$	$\nu(H_O)$	$\delta\nu(H_N)$	$\delta\nu(H_O)$			
en	218.62	187.38	—	186.98	—	+0.40	18.0	6.50	0.19
tn	216.12	184.88	215.72	184.37	+0.40	+0.51	18.3	6.83	0.12
dmen	220.44	188.31	—	187.80	—	+0.51	18.7	4.67	0.27
cis-$(NH_3)_2$	220.98	190.02	220.37	189.21	+0.61	+0.81	18.5	8.35	0.28
cis-py_2	234.04	187.96	234.65	186.38	−0.61	+1.58	18.8	6.20	0.24
phen	243.66	203.54	242.99	202.70	+0.67	+0.84	18.3	5.67	0.13

is reported[3,4,6] and consists of the malonate quartet at δ 3.38, a broad singlet at δ 2.75 due to methylene hydrogens of the coordinated ethylenediamine, and a broad peak at δ 5.12 due to the NH_2 group. The pyridine resonance of the *cis*-py_2 compound appears between δ 7.35 and 8.30, as reported previously (Fig. 3(d)).[8] The spectrum of the dmen compound consitsts of the methyl doublet (δ 2.07, $J\approx5$ Hz), a broad peak (δ 2.63) due to the methylene group, and a broad singlet (δ 5.53) due to the coordinated amine group, see Fig. 3(e). The methyl doublet collapsed into a singlet upon deuteration of the amine group. Figure 3(f) shows the spectrum of the phen compound and contains the phen multiplets between δ 7.50 and 8.90. In all the compounds, the malonate hydrogens appear as an AB quartet at around δ=3.1—4.1 and the J values assume almost constant values of about 18 Hz. The spectral parameters of these quartets (chemical shifts and J values) did not change with the solution pD. The AB quartet results from different magnetic environments seen by H_N and H_O.[3,4] The origin of this difference was discussed by Buckingham *et al.*[4] in connection with the conformation of malonate chelates. As shown in Table 1, the chemical shift differences between the H_N and H_O hydrogens are rather large, ranging from 30.96 Hz of the *cis*-$(NH_3)_2$ compound to 46.08 Hz of the *cis*-py_2 compound. Therefore, it is expected for all the compounds that the H_N hydrogen, for example, must be assigned either to the high-field pair of the quartet or the low-field counterpart. Several factors might be conceivable as the origin of the shift difference between H_N and H_O. They are the magnetic anisotropy of the central cobalt(III) ion and the anisotropic magnetic shielding of the C=O and C–O groups. The r^{-3} dependence of the former effect predicts[15] that the two hydrogens, H_N and H_O, more than 3.5 Å apart from the Co(III) ion of the *cis*-CoN_2O_4 chromophore do not exhibit the shift difference as large as 30 Hz (0.5 ppm), the value observed. The anisotropic shielding effect of the C=O and C–O groups of one malonate upon the chemical shift of the other malonate appears also unlikely, because the maximum shift difference observed for the Δ- and Λ-$[Co(ox)_2(R\text{-}pn)]^-$ pair is 0.16 ppm of the alpha hydrogen and the corresponding quantity in Δ- and Λ-$[Co(acac)_2(S\text{-}ala)]$ is 0.20 ppm.[16] The combined effect of the two COO groups within one malonate moiety would, however, amount to more than 0.6 ppm in some cases.[16d] It is rather difficult to assess quantitatively the shift difference since the shift difference of H_N and H_O depends critically on the conformation of the malonate chelate. The six-membered cobalt-malonate ring can adopt several conformation; the chair, boat, skew-boat, and intermediate stage conformations of these. The interconversion among these conformations will certainly be rapid, as discussed by Yoneda and Morimoto[3] and Buckingham *et al.*[4] In the absence of any other evidence, we can not decide the most stable conformation at present. Thus, it does not seem pertinent to discuss the chemical shift difference of H_N and H_O further.

The assignment of H_N, for example, to either the high-field or the low-field pair of the quartet will be made by comparing the chemical shift changes caused by changing nitrogen ligands. Among the en, tn, dmen, and *cis*-$(NH_3)_2$ complexes, the shift variations are relatively small and within 4.86 Hz for the low-field hydrogen and 5.14 Hz for the high-field one. For the compounds with aromatic ligands, we observed large shift variations, especially in the low-field pair. Thus, on going from the en compound to the *cis*-py_2 compound, we note that the chemical shift change of the low-field pair is 15.42 Hz while that of the high-field pair is 0.58 Hz. Likewise, the chemical shift differences between the en and phen complexes are 25.04 Hz and 16.16 Hz for the low- and the high-field pairs, respectively. The larger downfield shift of the low-field pair observed for aromatic ligands is probably due to the ring current effect[16d] of py and phen ligands and suggests that the hydrogen giving rise to the low-field pair is adjacent to the coordinating nitrogen. Therefore we propose that the hydrogen H_N undergoes a greater chemical shift change owing to its closeness to nitrogen ligands and is assigned to the low-field pair of the AB quartet.

To confirm the assignment, we have compared the chemical shift of $[Co(mal)_2(en)]^-$ and $[Co(mal)_2(meen)]^-$ ions, and of $[Co(mal)_2(gly)]^{2-}$ and $[Co(mal)_2(sar)]^{2-}$ ions.[17] In both pairs, the effect of *N*-methylation was greater for the low-field hydrogens than for the high-field ones. For example, the Meen compound exhibits two AB quartets due to malonate and the shift values of the high- and low-field hydrogens of one quartet are δ 3.11 and 3.62, respectively, and the corresponding values of the other quartet are δ 3.15 and 3.67. The latter values correspond nicely to the values

of the dmen compound (δ 3.14 and 3.67) so that this quartet is most probably due to the malonate CH_2 group adjacent to the *N*-methyl group of Meen. Thus the *N*-methylation of en caused a down-field shift of the low-field hydrogen by 0.03 ppm in both Meen and dmen compounds.

It should be pointed out that the present assignment of the AB quartet is opposite to the assignment of Farago and Smith.[6] Their assignment is based on the assumption that in the time averaged conformation of malonate-cobalt rings the H_N hydrogen is displaced, owing to the malonate-malonate repulsion, toward the NH_2 groups and is surrounded by more valence electrons than H_O. The high-field hydrogen is thus assigned to H_N. For reasons mentioned above, we do not favor their assignment.

In Table 1, the values of isotope shift[18] are also given. These values range from -0.61 to $+1.58$ Hz and they are of the magnitude usually observed.[18] In the *cis*-py_2 compound, a down-field isotope shift is found for the H_N hydrogen (-0.61 Hz). The H_O hydrogen of the same compound shows the usual upfield shift ($+1.58$ Hz). It will be interesting to note that stereochemically different hydrogens can show isotope shifts of opposite signs even if they are bonded to the same carbon atom. Generally, deuterium substitution

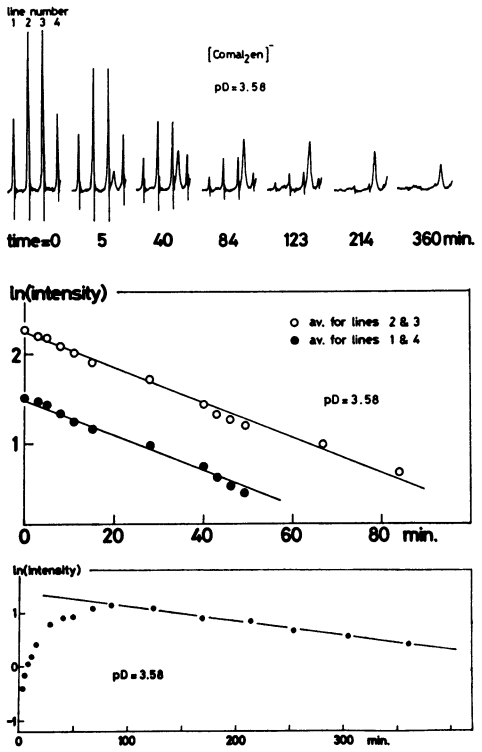


Fig. 4. An example of the kinetic analysis. The sample is $[Co(mal)_2(en)]^-$ at pD=3.58 and at 36.4 °C. (Top) The variation of the malonate portion of the spectrum with time, the H_O singlet being not numbered. (Mid-) dle) The ln (intensity) *vs.* time plots for the inner pair (lines 2 and 3, open circles) and the outer pair (lines 1 and 4, closed circles) of the quartet. (Bottom) The ln (intensity) *vs.* time plots of the H_O singlet. The solid line is the asymptote for the second stage of deuteration.

gem to a proton is reported to cause the proton resonance to be shifted upfield.[18] Only one exception is known to date; the NH_4^+ ion exhibited a downfield isotope shift.[19] This unusual isotope shift has been explained by electrostatic effects arising from hydrogen bonding with the polar deuterium oxide solvent. It appears that the isotope shifts of opposite sign exhibited by H_N and H_O of the *cis*-py_2 compound are reflecting different degrees of solvation around these hydrogens.

Stereoselectivity. The kinetic behavior expected from Eq. 4 to 7 is illustrated in Fig. 4 for the data of the en compound at pD=3.58. The top figure shows the time variation of the malonate portion of the spectrum. Immediately after dissolution we observed only the AB quartet, as expected for the presence of only H_N–C–H_O species. As time passes, the quartet decreases in intensity and at the same time a singlet appears exactly at the chemical shift of the high-field H_O hydrogen and grows in intensity with time. Then, the singlet begins to decrease in intensity and disappears eventually. The middle figure gives the time variation of the quartet intensity. In the figure, the natural logarithms of an average of the intensities of the inner and outer pair of the quartet are plotted against time by the open and closed circles, respectively. Both plots give straight lines and the slopes of both plots are the same within experimental uncertainties. Thus, the quartet intensity decreased exponentially with time over at least 2—3 half lives. As indicated by Eq. 4, these slopes correspond to k_Q or equally $k_{HN}+k_{HO}$. The bottom figure illustrates the time variation of the H_O singlet intensity. From this figure it appears rather difficult to obtain the initial rate constant, k_{HN} in this case. However, the second stage of deuteration follows the exponential law rather well, as indicated by the solid line in the figure. The slope of this asymptote corresponds to k_{HO}, as dictated by Eq. 6. The rate constant k_{HN} was obtained by $k_{HN}=k_Q-k_{HO}$, Eq. 5.

In the top figure we do not observe the H_N singlet due to the species H_N–C–H_O throughout the deuteration process. This means that the whole spectral change with time should be explained by the process

$$H_N\text{-C-}H_O \longrightarrow D\text{-C-}H_O \longrightarrow D\text{-C-}D,$$

where the species H_N–C–D was not produced during this deuteration process. Therefore, the deuteration takes place stereoselectively; the rate of deuteration of H_N is much larger than that of H_O.

The degree of the stereoselectivity can be defined by the ratio k_{HN}/k_{HO}. Qualitatively, the intensity ratio of the high- to low-field singlets can be taken as a rough measure of the degree of stereoselectivity. Figure 5 shows collectively the malonate portion of the NMR spectra of dmen, tn, *cis*-py_2, and phen compounds, taken some time after dissolution. The dmen and tn compounds exhibit marginally observable H_N singlet, in addition to the H_O singlet. This result indicates that the rate of deuteration of H_N is much faster than that of H_O in the dmen and tn compounds. The *cis*-py_2 and phen compounds show both H_N and H_O singlets in almost equal intensities, implying that the deuteration in these compounds proceeds with little or no stereoselectivity.

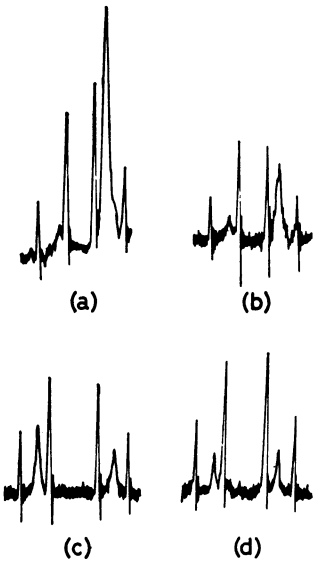


Fig. 5. The malonate portion of the NMR spectra of (a) dmen (pD=5.02), (b) tn (pD=7.18), (c) *cis*-py_2 (pD=6.55), and (d) phen (pD=6.02) complexes, taken some time after dissolution.

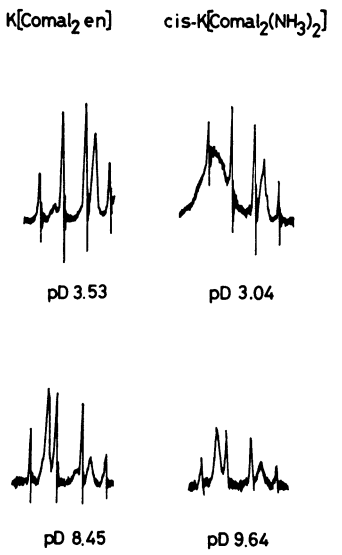


Fig. 6. The malonate portion of the NMR spectra of the en and *cis*-$(NH_3)_2$ compounds in acidified and basic deuterium oxide, taken some time after dissolution. The broad lump of the *cis*-$(NH_3)_2$ compound at pD= 3.04 is due to coordinated ammonia groups. This lump disappears in basic solution owing to the hydrogen-deuterium exchange at the ammonia groups.

Figure 6 illustrates the malonate portion of the NMR spectra of the en and *cis*-$(NH_3)_2$ compounds, taken some time after dissolution in acidified and basic deuterium oxide. At low pD, only the high-field H_O singlet can be observed for both compounds. At high pD, both the low-field H_N and the high-field H_O singlets are observed and the former is greater in intensity. These spectra are evidence that at low pD it is H_N that exchanges with deuterium first and at high pD it is H_O. Apparently the stereoselectivity in these two compounds is reversed on going from low to high pD region.

In Table 2, the second-order rate constants are given; the definition of these quantities is presented later. In terms of the second-order rate constants, the degree of the stereoselectivity is k'_{HN}/k'_{HO} or k''_{HN}/k''_{HO}. From Table 2, we see that while the degree of the stereoselectivity does not differ greatly for all the compounds in acid-catalysed reaction, it depends strongly upon the nitrogen ligand at high pD and is in the order (pD>8),

dmen > en, tn > *cis*-$(NH_3)_2$ > *cis*-py_2≈phen≈0

It is interesting to note that in *trans*-[Co(edda)(en)]$^+$ base-catalysed deuteration at glycine residues is more stereoselective than in acid-catalysed one.[20] It is reported that the degree of stereoselectivity is high and amounts to about 100 in the base-catalysis while it is about 10 in acid-catalysis.

Deuteration Mechanisms. The log(k) *vs.* pD plots for all the compounds are shown in Figs. 7 and 8, in which the deuteration rates of amine groups are also provided. The deuteration of amine groups is base-catalysed, as reported previously,[13] except for the *cis*-$(NH_3)_2$ compound at pD≈8. In other metal amine compounds, the hydrogen deuterium exchange reaction showed the first-order dependence on OD^- concentration in all instances.[13] This first-order dependence obtains even for systems where strong ion-pairing or stereoselective ion-association occurs between the amine group(s) and counter anions.[21] In the present systems,

Table 2. The second-order rate constants (s^{-1} mol^{-1} dm^3, 36.4 °C) for the deuteration of malonate hydrogens in bis(malonato)cobalt(III) complexes[a]

Ligand	Acid-catalysis			Base-catalysis			
	k'_Q	k'_{HN}	k'_{HO}	$k''_Q\times10^{-3}$	$k''_{HN}\times10^{-3}$	$k''_{HO}\times10^{-3}$	
en	1.4±0.8	(1.2)	0.2±0.1	38±20	(37)	1±0.6	pD<7
				1.3±0.7	0.25±0.14	(1.1)	pD>8
dmen	0.79±0.05	(0.7)	0.08±0.05	310±180	(300)	15±11	
tn	1.8±1.0	(1.6)	0.2±0.1	1±0.6	(0.8)	0.2±0.2	
cis-py_2	2.1±1.3	(1)[b]	(1)[b]	30±17	(15)[b]	(15)[b]	
phen	0.83±0.50	(0.4)[b]	(0.4)[b]	19±28	(10)[b]	(10)[b]	
cis-$(NH_3)_2$	3.2±3.0	(2.8)	0.4±0.3	0.55±0.32	0.32±0.14	(0.32)	pD>9

a) The values in parentheses are obtained by the relation; $k'_Q=k'_{HN}+k'_{HO}$ or $k''_Q=k''_{HN}+k''_{HO}$.b) Intensities of the H_N and H_O singlets are too small to allow rate measurements, but Fig. 5 indicates that k_{HN} is approximately equal to k_{HO}. Therefore these values are obtained on the assumption that $k_{HN}=k_{HO}$.

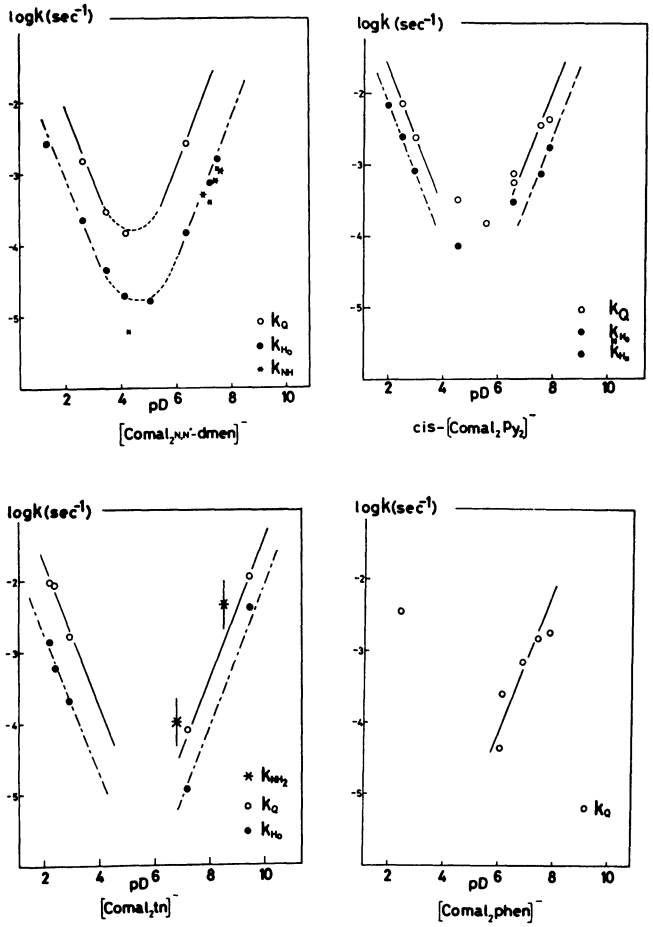


Fig. 7. The log(k) *vs.* pD plots for dmen, *cis*-py_2, tn, and phen complexes. The solid lines have a slope of $+1$ or -1.

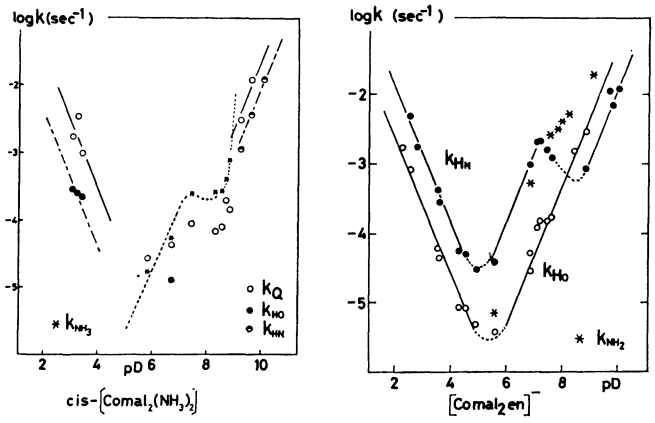


Fig. 8. The log(k) *vs.* pD plots for *cis*-$(NH_3)_2$ and en compounds. The solid lines have a slope of $+1$ or -1.

the compounds are singly-charged and it is safely assumed that the effect of ion-association upon amine exchange is minimal. The disparity found for the *cis*-$(NH_3)_2$ compound at pD$\approx$8 will be discussed later in connection with the reversal of the stereoselectivity.

It is seen that the deuteration of malonate groups is acid-catalysed at pD$<$4 and base-catalysed at pD$>$6. Thus, we have

$$k_i = k_i'[D_3O^+] + k_i''[OD^-] \quad (i = Q,\ H_N,\ \text{or}\ H_O)$$

where k_i' and k_i'' are the second-order rate constants for the acid- and base-catalysed reactions, respectively. Apparently, this first-order dependence on catalyst concentration is not obeyed again by the en and *cis*-$(NH_3)_2$ compounds in the region of pD 7 to 8 and this point will be discussed later. The D_3O^+ and OD^- concentrations are estimated by pD and $pK_{w(D_2O)} = 14.37$[12c] and the second-order rate constants are obtained. In Table 2, the second-order rate constants are summarized. They do not vary greatly from compound to compound at low pD, but in base-catalysed deuteration they differ significantly. At high pD, the value of k'' decreases in the order

$$\text{dmen} > \textit{cis}\text{-py}_2,\ \text{phen} > \text{en},\ \text{tn} > \textit{cis}\text{-}(NH_3)_2$$

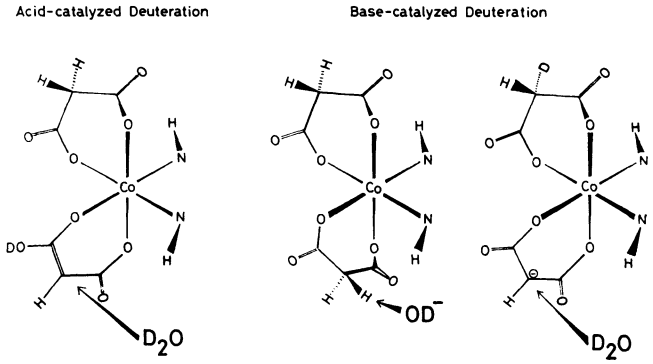
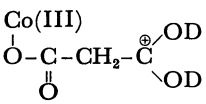


Fig. 9. A possible mechanism of acid- and base-catalysed deuteration that brings about stereoselectivity.

Mechanistically, acid-catalysed deuteration is effected by D_2O donating D^+ to the enol form, as depicted in Fig. 9. The enol results from the tautomerization of the protonated carbonyl form and is planar.[2,6] Therefore, if deuteration is to be stereoselective, it should take place preferentially either from the side adjacent to the coordinating amine group or from the side inbetween the two malonate groups. In the former case, H_N is deuterated first and we will observe the high-field H_O singlet. This is what we have found experimentally (*vide supra*).

In the acid-catalysed reaction, another mechanism will be considered. This mechanism is similar to the one proposed by Terrill and Reilley[22] for the deuteration of glycine residues in [Co(edta)]$^-$ ion. This involves the carbonyl protonation and subsequent rupture of the carboxylatocobalt bond. Since it assumes the unidentate carbonium ligand, such as



we may reasonably expect concomitant racemization at the metal center. For [Co(edta)]$^-$ ion, Terrill and Reilley in fact confirmed that deuteration is accompanied by racemization. To check the possibility of this mechanism, we resolved the en compound into optical isomers and measured the circular dichroism spectrum over the pH region of 2 to 12. Experimentally, however, we did not observe any measurable change in

the spectrum over the whole pH range and over several half lives of deuteration. This optical stability of the en compound corresponds well to the result of Dwyer *et al.*[9] It appears, therefore, that this mechanism is not appropriate at least to the en compound.

A probable mechanism of the base-catalysed deuteration is proposed previously.[2] It will suffice here to recall that the postulated mechanism involves the carbanion intermediate produced by hydrogen abstraction by OD^-. In the base-catalysed reaction, setereoselective deuteration may be effected in two ways; (a) hydrogen abstraction by OD^- is stereoselective, (b) deuteration by D_2O upon the carbanion intermediate is stereoselective. These two pathways are illustrated schematically in Fig. 9. Both processes may contribute to enhance the stereoselectivity if they occur from the N–H side(Note that the stereoselectivity is observed only for the amino-containing compounds.). It should be noted, however, that even if the hydrogen abstraction by OD^- had occurred stereoselectively, the resulting carbanion becomes most probably planar and loses its memory. The carbonion can be resonance stabilised with the adjacent carbonyl groups, which favors the planar structure. Further it is reported that retention of configuration has never been observed with simple carbanions.[23] Thus, (b) is considered the only likely process.

From the above, it is clear that the stereoselective deuteration in both acid- and base-catalysis is effected by D_2O donating D^+ to the enol and the carbanion intermediates, respectively. The present results indicate that at any pD the D_2O molecule prefers the access from the N–H side to that from the malonate side, except the high pD case of the en and *cis*-$(NH_3)_2$ compounds. The explanation of the stereoselectivity might be found in the conformation of the enol and carbanion intermediates. If the planar malonate moiety of these intermediates bends toward the coordinated nitrogen, steric repulsion is clearly expected between the amine group and the π-electron cloud of the enol or the unshared pair electron density of the carbanion. The planarity of these intermediates enforces the six-membered chelate ring to bend away from the coordinated nitrogen toward the other malonate-cobalt chelate. In this stable conformation of the intermediates, the access of D_2O molecule is likely to occur from the less-hindered side of coordinated nitrogen rather than from the more crowded malonate side.

Terrill and Reilley[22] made the variable temperature NMR studies on the stereoselective deuteration of $[Co(edta)]^-$. Sudmeier and Occupati[20] made a similar experiments on *trans*-$[Co(edda)(en)]^+$. For *trans*-$[Co(edda)(en)]^+$, $[Co(edta)]^-$, and their analogues,[24] the stereoselectivity was explained as the protection of a particular hydrogen from solvent molecules by the ethylenediamine backbone in the chelates. Farago and Smith[6] obtained the kinetic parameters for the deuteration of $[Co(mal)_2(en)]^-$ at about pD=3. This result is in good agreement with our data and indicated the stereoselectivity being entropy controlled. Further the data for the $[Co(mal)(en)_2]^+$ and $[Co(mal)(bpy)_2]^+$ ions pointed to the importance of the affinity of D_3O^+ or OD^- catalyst toward the ligands.

Origin of the Reversal of the Stereoselectivity. The reversal of the stereoselectivity as found for the en and *cis*-$(NH_3)_2$ compounds may be the most intersting aspect of the malonate exchange. In the $\log(k)$ *vs.* pD plots of Fig. 8, we note that the reversal takes place at about pD=7.5 and that the deuteration rates are retarded at around this pD. Concomitant with this anomalous pD dependence is the anomaly in the deuteration rate of coordinated amine groups. In the figure amine exchange rate is denoted by an asterisk. Above pD=8.5, a nomal first-order dependence of malonate exchange rates upon $[OD^-]$ obtains again. In the plots of the en compound, it is noteworthy that the rate of H_N is suppressed in the pD range of 7 to 8 and at pD=8, k_{HN} reverts to a $\log(k_{HN}) \propto +pD$ line whereas k_{HO} appears unaffected. If we note that the reversal is accompanied by anomalous decreases in both malonate and amine exchange rates, the amine exchange may be considered to play an important role in this phenomenon. The *cis*-py_2 and phen compounds lack exchangeable N–H groups. Though the dmen and tn compounds do have these groups, their exchange rates are slower than or at most similar to those of the malonate exchange in each complex. The NH_2 resonance of the tn compound overlapped with a strong solvent HDO signal as seen in Fig. 3(b), which precluded accurate rate measurements. For *cis*-$(NH_3)_2$ compounds, it appears that the reversal of stereoselectivity takes place at such a pD value that the rate of amine exchange exceeds significantly that of malonate exchange. At this pD value, both amine and malonate hydrogens may be considered to have become equally reactive so that they might well compete for the OD^- catalyst. As a result, it is probable that both rates tend to fall together.

In the plots of the en compound, the anomaly of the amine exchange rate is less prominent than that of the malonate exchange rate. The point to be noted here is that the amine exchange rate is close to but slower than the malonate exchange even at the pD value where the k_{HN} begins to be suppressed. This observation suggests that though amine exchange does pertain in some way to the reversal, but it is not the only cause for the reversal. Some probable factors other than competition for the OD^- catalyst might be invoked. For example, one may consider the possibility that the amine and malonate hydrogens are exchanging between themselves in the pD region of 7 to 9. Under such conditions, both amine and malonate exchange rates might well be suppressed since these hydrogens are not exchanging with solvent deuterium but among themselves. By dissolving the en compound in acidified D_2O and precipitating with dry dioxane after suitable time intervals, we obtained the partially deuterated compound $K[Co(mal\text{-}d_2)_2(en)]$, for which only the malonate is deuterated completely leaving the amine group undeuterated. If the abovementioned intramolecular exchange is present, we may observe the malonate resonance to grow with time by dissolving this partially deuterated compound in D_2O at pD$\geqq$7.5. This is because the amine hydrogens that survived the partial deuteration are going to be transferred to the malonate.

We have not, however, succeeded in detecting the expected malonate resonance despite our repeated trials. We are therefore inclined to regard this intramolecular hydrogen exchange less probable. One may consider, further, that the conformation of the malonate ring changes at around pD=7 specifically in the en and *cis*-$(NH_3)_2$ compounds. It is well known[25] that conformational changes of chelate rings often show up as a change of circular dichroism spectrum. To check this possibility we have resolved the en compound into optical isomers and measured the circular dichroism spectrum over the pD range of 2 to 11. However, the circular dichroism spectrum of the optically resolved en compound exhibited no change against pD, rendering the conformational change also unlikely.

After all, our explanation at this stage is that at this pD region amine and malonate hydrogens compete for the OD^- catalyst for some reasons. In order for this process to occur, some stereochemical condition should be fulfilled. In the plots of the en compound of Fig. 8, only the rate of H_N hydrogen, which is adjacent to the amine group, is retarded while that of the H_O hydrogen, which is situated farthest apart from the amine group, remains unaffected. This will be taken to suggest that stereochemically close and, in addition, equally reactive groups are allowed to interfere with each other's exchange.

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5) Abbreviations; mal=malonate dianion, en=ethylenediamine, tn=1,3-propanediamine, dmen=*N*,*N*-dimethylethylenediamine, phen=1,10-phenanthroline, bpy=2,2′-bipyridine, edta=ethylenediaminetetraacetate anion, ox=oxalate anion, pn=1,2-propanediamine, acac=acetylacetonate anion, ala=alaninate anion, gly=glycinate anion, meen=*N*-methylethylenediamine, sar=*N*-methylglycine, py=pyridine.

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