Role of Substituents in Copper(II) Extraction with *N,N'*-Bis(8-quinolyl)malonamides

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It has been found that substituents on *N,N'*-bis(8-quinolyl)malonamide play an important role in copper(II) extraction: among the substituents studied, benzyl groups dramatically increased extractability of the malonamide complex. The role of substituents is discussed on the basis of the results of titration and ^{1}H NMR measurements of copper(II) or nickel(II) complexes as well as copper(II)-extraction experiments. Intramolecular interactions between π electrons of the benzyl group and the metal centre of the complex are proposed to occur.

Intensive study of molecular recognition in biological systems has shown that weak inter- and intra-molecular interactions play important roles.[1] Understanding of molecular recognition by skilful modification of weak interactions is a fascinating subject from the viewpoint of model studies of biological function and in the development of new functionalized compounds.[2–4] Recently it has been recognized that some functions of metal ions in biomaterials can be ascribed to weak interactions such as hydrogen bonding, Coulomb or van der Waals forces. Therefore, much attention has been paid to metals in biomaterials, and model metal complexes have been designed to mimic these.[5] Yamauchi and co-workers[6] reported that interactions between aromatic rings play an important role in stabilizing ternary metal complexes of amino acids and chelating nitrogen ligands. In a series of their studies, effects of stacking of aromatic rings upon rates of complex formation, stability and adopted conformations have been investigated by modification of the aromatic rings upon incorporation of substituents. The properties of metal ion-organic complexes have also been reported to be affected by stacking of aromatic rings and by interactions between metal ions and aromatic rings.[7] In binary systems, however, it seemed rather difficult to study systematically effects of the variation of the structure of aromatic rings on the properties of the resulting complexes.

Recently, we have synthesised several tetradentate ligands derived from *N,N'*-bis(8-quinolyl)malonamide and have studied their metal-complexation and -extraction abilities.[8,9] The malonamides are easily synthesised from a versatile starting material, ethyl malonate, in several steps. Di-*n*-butyl-*N,N'*-bis-(8-quinolyl)malonamide (H_2L^1), forms 1:1 complexes with several transition metals with simultaneous release of both amide protons.[8] Ligand H_2L^1 can selectively extract Cu^{II} from aqueous solutions containing other divalent metal ions such as Ni^{II}, Co^{II} and Zn^{II} into chloroform under neutral or weakly acidic conditions. The divalent metal ions are presumed to be centrally co-ordinated within the complexes by two amide and two quinolyl nitrogen atoms.[9] A copper(II)-selective macrocyclic chelating agent, 1,4,8,11-tetraazacyclotetradecane-5,7-dione in which Cu^{II} is also centrally co-ordinated, has been previously reported.[10]

Herein are reported the metal-complexation and -extraction properties of a series of *N,N*-bis(8-quinolyl)malonamide derivatives.

Experimental

General.—Proton NMR spectra were recorded at 300 MHz on a Bruker MSL-300 spectrometer. Chemical shifts are reported *vs.* $SiMe_4$. UV/VIS measurements were performed on a Hitachi 330 spectrophotometer.

Infrared spectra were recorded with a JASCO A-3 spectrometer (resolution ± 5 cm^{-1}). Precise mass and secondary-ion mass (SIMS) spectra were measured by a Hitachi M80BS spectrometer. The concentrations of metal ions in the extraction experiments were determined on a Shimadzu AA-646 atomic absorption spectrometer. Melting points were measured with a Mitamura Riken microscope.

Materials.—All reagents were supplied by Wako or Kanto Chemical Companies. Benzene was dried over molecular sieves (4 Å) or distilled from CaH_2 prior to use. Triethylamine was distilled from potassium hydroxide. All other reagents and solvents were used as received. Silica gel for column chromatography was Wakogel C300.

Synthesis of N,N'-*Bis*(8-*quinolyl*)*malonamide Derivatives.*—*General procedure.* To a solution of diethyl malonate (0.1 mol) in dry tetrahydrofuran (200 cm^3) was added an equimolar amount of NaH powder under stirring at room temperature. To the resulting clear solution, alkyl bromide (0.1 mol) was added and the reaction mixture was refluxed for 24 h. After cooling to room temperature, further NaH (0.1 mol) was added and the mixture allowed to stir for *ca.* 4 h. Further alkyl bromide (0.1 mol) was added to the solution and refluxed for 24 h. For the synthesis of the mixed benzyl cyclohexylmethyl derivative the monosubstituted benzyl diethyl malonate was isolated as usual, purified by distillation, and then treated with an equivalent of cyclohexylmethyl bromide. After removal of the solvent under reduced pressure, diethyl ether (300 cm^3) was added to the residue and the solution was washed with water (3 × 200 cm^3) and dried over $MgSO_4$. After evaporation of the solvent, the residue was distilled *in vacuo* to give the disubstituted diethyl malonate. The ester was hydrolysed under basic conditions (KOH in aqueous ethanol) and was treated in the usual manner to give the disubstituted malonic acid.

Disubstituted malonic acid (0.01 mol) and excess of thionyl chloride (5 cm^3, 0.0685 mol) were stirred at 60 °C for *ca.* 4 h

Table 1 Physical data of malonamide derivatives

Compound	R	R′	Yield (%)	M.p./°C	M^+ (m/z)[a]	ν(NH)/cm^{-1}	ν(C=O)/cm^{-1}	λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})[b]
H_2L^1	Bu	Bu	81	142–143	468.251(468.252)	3300	1680	321(13 500)
H_2L^2	$C_6H_{11}CH_2$	$C_6H_{11}CH_2$	70	205–209	548.313(548.315)	3340	1680	321(12 900)
H_2L^3	$C_6H_{11}CH_2$	$PhCH_2$	63	198–200	542.266(542.268)	3380, 3320	1680	320(14 200)
H_2L^4	$PhCH_2$	$PhCH_2$	71	238–239	536.221(536.221)	3300	1680	320(14 900)
H_2L^5	p-$MeC_6H_4CH_2$	p-$MeC_6H_4CH_2$	67	155–159	564.252(564.252)	3300	1675	321(13 600)
H_2L^6	$PhCH_2CH_2$	$PhCH_2CH_2$	78	144–146	564.249(564.252)	3340	1680	320(11 200)
H_2L^7	$PhCH_2CH_2CH_2$	$PhCH_2CH_2CH_2$	68	118–119	592.285(592.284)	3325	1675	321(13 200)

[a] Required values given in parentheses. [b] In $CHCl_3$.

Table 2 NMR data of malonamide derivatives*

Compound	H^2	H^3	H^4	H^5	H^6	H^7	NH	Other
H_2L^1	8.88	7.46	8.15	7.52	7.56	8.90	11.32	0.89 (t) (7.0), CH_3
	(dd)	(dd)	(dd)	(dd)	(t)	(dd)	(s)	1.42 (m), $CH_2(CH_2)_2CH_3$
	(4.2, 1.5)	(8.3, 4.2)	(8.3, 1.6)	(8.2, 1.5)	(8.1)	(7.3, 1.5)		2.31 (m), $CH_2(CH_2)_2CH_3$
H_2L^2	8.93	7.47	8.17	7.53	7.58	8.91	11.66	1.00, 1.47, 1.77 (m, C_6H_{11})
	(dd)	(dd)	(dd)	(dd)	(t)	(dd)	(s)	2.24 (d) (6.2), CH_2
	(4.0, 1.7)	(8.2, 4.2)	(8.3, 1.6)	(8.2, 1.7)	(8.2)	(7.0, 1.7)		
H_2L^3	8.86	7.44	8.16	7.53	7.58	8.89	11.50	1.04, 1.51, 1.78 (m, C_6H_{11})
	(dd)	(dd)	(dd)	(dd)	(t)	(dd)	(s)	2.37 (d) (6.3), $CH_2C_6H_{11}$)
	(4.2, 1.7)	(8.3, 4.2)	(8.3, 1.7)	(8.3, 1.9)	(8.2)	(7.1, 1.9)		3.61 (s), CH_2Ph
								6.99 (m), Ph, 7.16 (m), Ph
H_2L^4	8.78	7.42	8.41	7.52	7.56	8.88	11.41	3.76 (s), CH_2
	(dd)	(dd)	(dd)	(dd)	(t)	(dd)	(s)	7.04 (m), Ph
	(4.2, 1.6)	(8.2, 4.2)	(8.3, 1.6)	(8.3, 2.0)	(8.2)	(7.0, 2.0)		
H_2L^5	8.79	7.42	8.14	7.53	7.57	8.88	11.41	2.09 (s), CH_3
	(dd)	(dd)	(dd)	(dd)	(t)	(dd)	(s)	3.70 (s), CH_2
	(4.2, 1.6)	(8.2, 4.2)	(8.2, 1.6)	(8.2, 2.0)	(8.2)	(7.0, 2.0)		6.82 (d) (7.9), $MeC_6H_4CH_2$
								7.12 (d) (8.0), $MeC_6H_4CH_2$
H_2L^6	8.92	7.49	8.18	7.56	7.59	8.59	11.50	2.68 (m), CH_2CH_2Ph
	(dd)	(dd)	(dd)	(dd)	(t)	(dd)	(s)	2.83 (m), CH_2CH_2Ph
	(4.2, 1.6)	(8.3, 4.2)	(8.3, 1.6)	(7.9, 1.9)	(8.2)	(6.8, 2.0)		7.1–7.3 (m), Ph
H_2L^7	8.83	7.45	8.15	7.52	7.56	8.86	11.21	1.75 (m), $CH_2CH_2CH_2Ph$
	(m)	(dd)	(dd)	(dd)	(t)	(m)	(s)	2.33 (m), $CH_2CH_2CH_2Ph$
		(8.3, 4.2)	(8.3, 1.5)	(8.3, 1.8)	(8.3)			2.69 (m), $CH_2CH_2CH_2Ph$

* Data given as chemical shift (δ), multiplicity, J/Hz; s = singlet, d = doublet, t = triplet and m = multiplet.

under Drierite. After removal of excess of thionyl chloride under reduced pressure, the residue was dried *in vacuo*. It was then dissolved in benzene (20 cm^3) and 8-aminoquinoline (2.9 g, 0.02 mol) was added. The resulting bright orange precipitate was stirred at room temperature under Drierite for 1 h. Triethylamine (0.02 mol) was then added and the reaction mixture immediately bleached and became thicker. After stirring overnight at 60 °C, it was washed with water (3 × 20 cm^3). The organic layer was dried over $MgSO_4$, filtered, and the solvent was evaporated. The resulting solid was purified by chromatography on silica gel (200 g) with chloroform. Crystalline compounds were obtained by crystallization from cyclohexane. Physical characteristics and NMR data for all the new malonamide derivatives are given in Tables 1 and 2, respectively.

Synthesis of Metal Complexes of Malonamides.—Copper(II) *complexes of* N,N′-*bis*(8-*quinolyl*)*malonamide derivatives.* Copper(II) acetate monohydrate (0.1 g, 0.5 mmol) in ethanol (7 cm^3) was added to an EtOH solution (15 cm^3) of the *N*,*N*′-bis-(8-quinolyl)malonamide derivative (0.2 mmol). The colour of the reaction mixture turned greenish brown. Removal of the solvent under reduced pressure left a residue which was crystallized from benzene or cyclohexane–benzene and dried *in vacuo*. The yield of the copper(II) complex of the dibutyl malonamide H_2L^1 was improved from that reported previously.[9]

Nickel(II) *complexes of* N,N′-*bis*(8-*quinolyl*)*malonamide derivatives.* Nickel(II) acetate tetrahydrate (0.1 g, 0.4 mmol) in ethanol (10 cm^3) was added to an EtOH solution (15 cm^3) of the *N*,*N*′-bis(8-quinolyl)malonamide derivative (0.2 mmol). The colour of reaction mixture turned deep red. Evaporation of the solvent left a dark green solid residue which was recrystallized from hot ethanol. The dark green crystals were washed with cold ethanol and dried *in vacuo*. Another crop could be recovered from the mother-liquor. The product could also be recrystallized from benzene or cyclohexane–benzene and dried *in vacuo*.

Physical characteristics of the copper- and nickel-(II) complexes of the malonamide derivatives H_2L^1–H_2L^7 are given in Table 3 and NMR data for the nickel(II) complexes are given in Table 4.

General Procedure of Solvent Extraction.—Into a sample tube (20 cm^3) with a screw cap were poured an aqueous solution (5 cm^3) containing either, each of, or a mixture of transition-metal ions (Cu^{II}, Ni^{II}, Co^{II} and Zn^{II} each 1 mmol dm^{-3}) and a chloroform solution (5 cm^3) containing a diamide derivative (1 mmol dm^{-3}) and the mixture was shaken vigorously for 24 h at 25 °C. The concentration of the remaining metal ions in aqueous solution was determined by atomic absorption spectroscopy, from which the concentration of metal ions extracted into chloroform could be determined. The aqueous solution adjusted to pH 6.2 was prepared from NaO_2CMe (39.5 cm^3, 1 mol dm^{-3}) and $MeCO_2H$ (5 cm^3, 0.2 mol dm^{-3}) (total amount of solution 1 l). In order to estimate the stability of metal complexes, aqueous solutions adjusted to pH 1.4, 2.6, 3.2, 3.8, 4.3 or 5.2 were prepared from NaO_2CMe (50 cm^3, 1 mol dm^{-3}) and 60, 50, 47, 40, 30 or 10 cm^3 of 1 mol dm^{-3} HCl, respectively

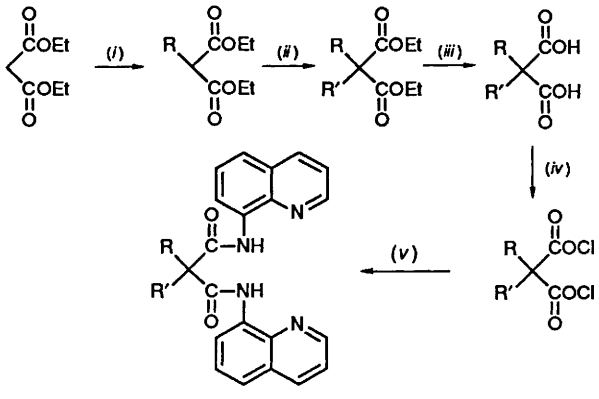
Table 3 Physical data of metal complexes of malonamide derivatives

Compound	R	R′	Yield (%)	M.p./°C	$(M + 1)^+$ $(m/z)^a$	ν(C=O)/cm^{-1}	λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})^b
[NiL^1]	Bu	Bu	82	294–297	525.3(525.4)	1630	442(8900)
[CuL^1]	Bu	Bu	86	275–277	531.0(531.1)	1620	406(7100)
[NiL^2]	$C_6H_{11}CH_2$	$C_6H_{11}CH_2$	67	302–304	605.4(605.5)	1620	442(8900)
[CuL^2]	$C_6H_{11}CH_2$	$C_6H_{11}CH_2$	71	316–318	611.0(611.3)	1620	406(7100)
[NiL^3]	$C_6H_{11}CH_2$	$PhCH_2$	75	237–240	599.4(599.5)	1610	441(7000)
[CuL^3]	$C_6H_{11}CH_2$	$PhCH_2$	80	230–232	605.0(605.2)	1610	406(7300)
[NiL^4]	$PhCH_2$	$PhCH_2$	83	320–322	593.2(593.4)	1650	440(8800)
[CuL^4]	$PhCH_2$	$PhCH_2$	85	306–309	598.8(599.2)	1600	402(6000)
[NiL^5]	*p*-$MeC_6H_4CH_2$	*p*-$MeC_6H_4CH_2$	69	307–308	621.5(621.5)	1600	443(8600)
[CuL^5]	*p*-$MeC_6H_4CH_2$	*p*-$MeC_6H_4CH_2$	77	297–299	626.4(626.8)	1515	405(6400)
[NiL^6]	$PhCH_2CH_2$	$PhCH_2CH_2$	81	245–247	621.5(621.5)	1600	442(8300)
[CuL^6]	$PhCH_2CH_2$	$PhCH_2CH_2$	84	272–274	626.7(626.8)	1595	405(6700)

^{a} Required values given in parentheses. ^{b} In $CHCl_3$.

Table 4 NMR data of nickel(II) complexes of malonamide derivatives

Compound	H^2	H^3	H^4	H^5	H^6	H^7	Other
[NiL^1]	7.83	7.44	8.31	7.29	7.57	9.09	0.81 (t) (7.0), CH_3
	(d)	(dd)	(d)	(d)	(t)	(d)	1.32 (m), $CH_2(CH_2)_2CH_3$
	(4.9)	(8.1, 5.1)	(8.1)	(8.1)	(8.0)	(8.0)	2.05 (m), $CH_2(CH_2)_2CH_3$
[NiL^2]	7.92	7.46	8.34	7.33	7.61	9.01	0.97, 1.4–1.5 (m), C_6H_{11}
	(d)	(dd)	(d)	(d)	(t)	(d)	1.96 (d), CH_2
	(4.8)	(8.1, 5.1)	(8.1)	(7.9)	(8.0)	(7.9)	
[NiL^3]	7.60	7.33	8.26	7.27	7.58	8.97	1.08, 1.56, 1.84 (m), C_6H_{11}
	(d)	(dd)	(d)	(d)	(t)	(d)	2.22 (d) (6.7), $CH_2C_6H_{11}$
	(5.0)	(8.2, 5.2)	(8.2)	(8.0)	(8.0)	(8.0)	3.23 (s), CH_2Ph, 7.12 (m), Ph
[NiL^4]	7.35	7.12	8.11	7.18	7.50	8.90	3.50 (s), CH_2
	(d)	(dd)	(d)	(d)	(t)	(d)	6.87 (m), Ph
	(5.2)	(8.2, 5.2)	(8.1)	(8.0)	(8.0)	(7.9)	7.30 (m), Ph
[NiL^5]	7.42	7.19	8.16	7.19	7.53	8.92	2.01 (s), CH_3
	(d)	(m)	(d)	(m)	(t)	(d)	3.45 (s), CH_2
	(5.0)		(8.1)		(8.0)	(7.8)	6.70 (d) (7.9), $MeC_6H_4CH_2$
							7.19 (d) (7.7), $MeC_6H_4CH_2$
[NiL^6]	7.92	7.47	8.36	7.36	7.64	9.14	2.42 (m), CH_2CH_2Ph
	(d)	(dd)	(d)	(d)	(t)	(d)	2.71 (m), CH_2CH_2Ph
	(5.1)	(8.2, 5.2)	(8.2)	(8.0)	(8.0)	(8.0)	7.03–7.23 (m), Ph
[NiL^7]	7.78	7.40	8.29	7.31	7.59	9.08	1.70 (m), $CH_2CH_2CH_2Ph$
	(d)	(dd)	(d)	(d)	(t)	(d)	2.16 (m), $CH_2CH_2CH_2Ph$
	(5.1)	(8.2, 5.2)	(8.2)	(8.1)	(8.0)	(8.0)	2.61 (m), $CH_2CH_2CH_2Ph$
							7.08 (m), Ph



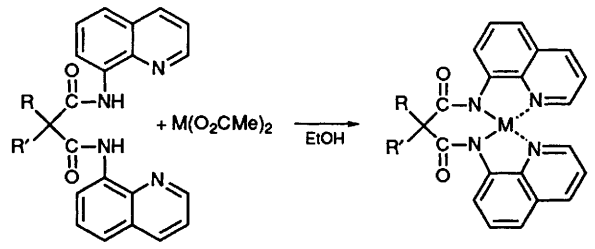
Scheme 1 R,R′ = Bu, $C_6H_{11}CH_2$, $PhCH_2$, *p*-$MeC_6H_4CH_2$, $PhCH_2CH_2$ or $PhCH_2CH_2CH_2$: (*i*) NaH, RBr; (*ii*) NaH, R′Br; (*iii*) KOH, aqueous EtOH then HCl(aq); (*iv*) $SOCl_2$; (*v*) 8-aminoquinoline, NEt_3–C_6H_6

(total amount of each solution 250 cm^3) and pH 5.9 from NaO_2CMe (38 cm^3, 1 mol dm^{-3}) and $MeCO_2H$ (10 cm^3, 0.2 mol dm^{-3}) (total amount of solution 200 cm^3). The extraction experiments were then performed as above and the concentration of the extracted metal ions determined at each pH value.

Titration Experiments.—A dioxane–water (7:3 v/v) solution of the *N*,*N*′-bis(8-quinolyl)malonamide derivative (0.1 mmol dm^{-3}) and $CuSO_4$ (10 mmol dm^{-3}) was adjusted to pH ≈ 1.6 with 1 mol dm^{-3} HCl solution. To the solution (100 cm^3) were added determined amounts of 1 mol dm^{-3} NaOH solution and the change of pH measured. The UV/VIS spectrum was measured at each pH value (at 400 nm) and the concentration of the copper(II) complex of the malonamide derivative determined.

Results and Discussion

Synthesis of Malonamide Derivatives.—*N*,*N*′-Bis(8-quinolyl)-malonamide derivatives with a variety of substituents were easily synthesised in good yields by the procedure shown in Scheme 1. Disubstituted *n*-butyl (H_2L^1), cyclohexylmethyl (H_2L^2), benzyl (H_2L^4), *p*-methylbenzyl (H_2L^5), 2-phenylethyl (H_2L^6) and 3-phenylpropyl (H_2L^7) derivatives were prepared which were chosen to enable substituent effects to be studied systematically. A mixed cyclohexylmethyl benzyl derivative (H_2L^3) was also prepared. The malonamide derivatives were characterized by 300 MHz ^{1}H NMR, IR and UV/VIS spectroscopy and by precise mass spectrometry. As seen in Table 1, the spectroscopic data of these malonamide derivatives are very similar. In their ^{1}H NMR spectra (Table 2) chemical shift differences for corresponding amide and quinolyl protons are within 0.03 ppm in all cases. The introduction of substituents thus results in no evident spectral changes in the 8-quinolylamido moiety.



Scheme 2 M = Cu^{II} or Ni^{II}

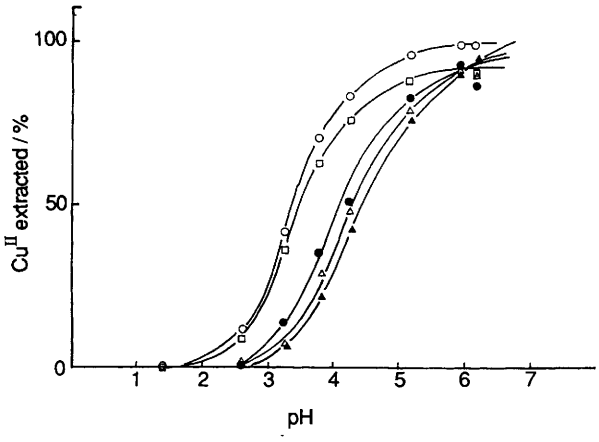


Fig. 1 pH Dependence of copper(II) extraction of malonamide derivatives: R = R′ = $PhCH_2$ (H_2L^4) (○); $PhCH_2CH_2$ (H_2L^6) (●); $PhCH_2CH_2CH_2$ (H_2L^7) (△); Bu (H_2L^1) (▲); and *p*-$MeC_6H_4CH_2$ (H_2L^5) (□)

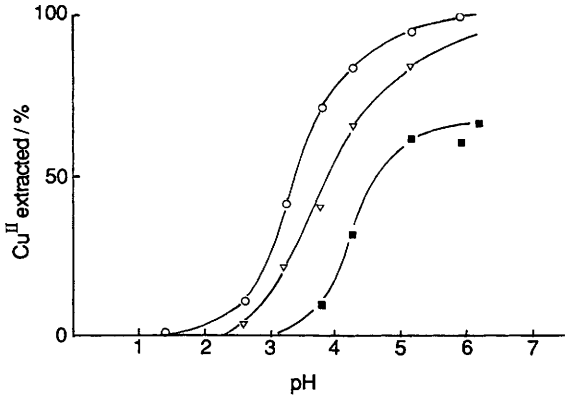


Fig. 2 Effect of the benzyl group on the pH dependence of copper(II) extraction of malonamide derivatives: R = R′ = $PhCH_2$ (H_2L^4) (○); R = R′ = $C_6H_{11}CH_2$ (H_2L^2) (■); and R = $C_6H_{11}CH_2$, R′ = $PhCH^3{}_2$ (H_2L^2) (▽)

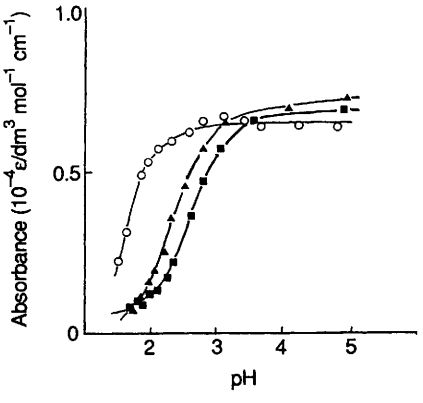


Fig. 3 Plot of absorbance (λ = 400 nm) *vs.* pH for copper(II)–malonamide derivatives in water–dioxane (3:7 v/v): R,R′ = $PhCH_2$ ([CuL^4]) (○); Bu([CuL^1]) (▲); and $C_6H_{11}CH_2$([CuL^2]) (■)

Preparation of Metal Complexes of Malonamide Derivatives.—Di-*n*-butyl-*N*,*N*′-bis(8-quinolyl)malonamide H_2L^1 has been reported to form 1:1 complexes with Cu^{II}, Ni^{II}, Zn^{II}, Cd^{II} and Pd^{II}.[9] In this study, only copper- and nickel-(II) complexes were prepared from the newly synthesised malonamides. Both copper- and nickel-(II) acetate easily reacted with each malonamide in solution with deprotonation of the amide groups (Scheme 2). They were characterized by ^1H NMR, IR and UV/VIS spectroscopy and by SIMS and the data are summarized in Tables 3 and 4. No evident differences in IR and UV spectral data were noted for the complexes indicating a similar structure for all of them with a 1:1 stoichiometry in each case.

Effect of Substituents on Copper(II) Extraction.—As reported previously[8] for H_2L^1, all the new malonamides H_2L^2–H_2L^7 extracted Cu^{II} exclusively into chloroform from an aqueous mixture of Cu^{II}, N^{II}, Co^{II} and Zn^{II}. Under the present conditions, all the other metal ions remained in the aqueous layer. Although extractability of these malonamides was also examined with each ion singly (Cu^{II}, Ni^{II}, Co^{II} and Zn^{II}), only copper(II) extraction was observed. Nickel(II) was not extracted at all even when the concentration of Ni^{II} in the aqueous layer was increased to 10 times that of the extractant.

The pH dependence of extractability was examined. Fig. 1 shows the amounts of extracted Cu^{II} at different pH values after 1 d after equilibrium had been attained (for H_2L^2 this required 2 d). The extraction curves can be classified roughly into two groups with malonamides H_2L^4 and H_2L^5 having benzyl or *p*-methylbenzyl groups extracting Cu^{II} at lower pH values. By contrast, the other malonamides only start to extract Cu^{II} at about a unit higher pH.

Extraction of metal ions from aqueous solution into an organic phase requires both an interaction of the extractant with metal ions at the water–organic solvent interface and stability of the metal complex in the organic solvent. The origin of the differing behaviour of the benzyl and *p*-methylbenzyl derivatives relative to the phenylethyl or phenylpropyl derivatives is probably not due to hydrophobicity or bulkiness considerations as these are similar for all these substituents. One clear difference however shown by molecular model (Corey–Pauling–Koltun) examinations of these malonamides is the degree of steric hindrance around the α-carbon. Owing to the short $-CH_2-$ spacer, rotation around the α-carbon is restricted for the benzyl and *p*-methylbenzyl groups while for butyl, phenylethyl or phenylpropyl groups with longer alkyl chains this does not arise. This factor could provide an explanation for the differing extractability of these malonamides. Interestingly, the bis(cyclohexylmethyl) derivative (H_2L^2), which like H_2L^4 and H_2L^5 would show restricted rotation about the α-carbon, shows the lowest extractability (Fig. 2) and slowest attainment of equilibrium. While steric factors are expected to be the main reason for the slow extraction rate (the cyclohexylmethyl group is bulkier than the benzyl group) the difference in extractability seems too much to be caused by this factor alone. Significantly extractability is improved substantially when a benzyl group is substituted for one of the two cyclohexylmethyl groups of H_2L^2 as shown in Fig. 2. In order further to investigate differences in extractability of copper(II), titration experiments of some malonamides were undertaken. In addition, diamagnetic, square-planar nickel(II) complexes of H_2L^1–H_2L^7 were prepared and their ^1H NMR spectroscopic behaviour studied.

Effects of Substituents on Titration Behaviour.—All of the malonamides used in this study are so lipophilic that both they and their metal complexes are insoluble in water. Therefore the pH-titration experiments were performed in dioxane–water (7:3 v/v). The amount of the complex formed was determined by UV/VIS spectroscopy at 400 nm at a variety of pH values for the mixed solution. As seen in Fig. 3, the pH–UV/VIS absorbance curves can also be grouped in two with the malonamide

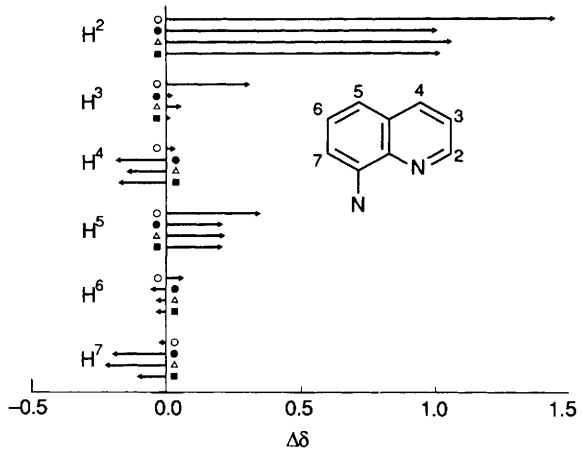


Fig. 4 Change in chemical shift (Δδ) of quinolyl protons upon complexation of the malonamide derivatives to nickel(II): R,R′ = $PhCH_2$ ([NiL^4]) (○); $PhCH_2CH_2$ ([NiL^6]) (●); $PhCH_2CH_2CH_2$ ([NiL^7]) (△); and $C_6H_{11}CH_2$ ([NiL^2]) (■)

derivatives having benzyl or *p*-methylbenzyl substituents, H_2L^4 and H_2L^5, forming complexes at lower pH values than the others. This indicates higher stability for the copper(II) complexes of H_2L^4 and H_2L^5 and is in accord with the results of the extraction experiments.

Proton NMR Spectroscopic Behaviour of the Nickel(II) Complexes.—In order to investigate the behaviour of metal complexes of malonamides, especially the effect of the introduction of substituents, ^1H NMR spectra were measured for $CDCl_3$ solutions of the nickel(II) complexes. From Tables 2 and 4, it can be seen that the difference of chemical shifts for corresponding protons between the malonamide derivatives and their nickel(II) complexes (Δδ) is substituent dependent with generally Δδ values for the malonamide complexes having benzyl or *p*-methylbenzyl group being larger. Fig. 4 shows the relative Δδ values for quinolyl group protons for the benzyl, 2-phenylethyl, 3-phenylpropyl and cyclohexylmethyl derivatives. Very similar Δδ values are observed for a given proton for all the studied systems except for the benzyl and *p*-methylbenzyl derivatives. The specific NMR behaviour of malonamides having benzyl or *p*-methylbenzyl groups mirrors their distinct behaviour in copper(II) extraction experiments.

The crucial role of the benzyl group in the stabilization and conformations of metal complexes and several biomaterials has been established previously. Yamauchi and co-workers[6] have also reported that the π electrons of an intramolecular benzyl group are important in stabilizing ternary metal complexes containing amino acids and chelating nitrogen ligands. An interaction between the benzyl group and the metal centre or the quinolyl group is proposed for the interpretation of the present results. For the nickel(II) benzyl derivative, [NiL^4], for example, the H^2 proton of the quinolyl group shifts by ≈1.4 ppm upfield relative to the free ligand, some 0.4 ppm more than the shift for the remainder of the complexes. Reference to Fig. 4 reveals similar anomalous behaviour for H^{3-5} and H^7. These results indicate an interaction of the benzyl group with the remainder of the complex. The interaction of the π electrons of the benzyl group could be either with the metal (π-back donation) or the quinolyl groups (π–π ring current) both of which could explain the observed upfield shifts. However, given that the upfield shift of H^4 is observed as well as those of other protons this behaviour could not be explained by a benzyl–quinolyl interaction owing to the large spatial separation of proton H^4 and the benzyl group, as established by a Corey–Pauling–Koltun molecular model. Therefore, an interaction between the π electrons and the metal seems to be the most plausible explanation of the spectroscopic data. Higher steric hindrance around the α-carbon may be advantageous for a stable intramolecular interaction between the benzyl groups and a metal ion owing to reduced mobility. On the other hand, the presence of flexible alkyl spacer chains disturbs intramolecular interactions between the metal ion and π electrons of phenylethyl or phenylpropyl groups.[7]

Conclusion

From the liquid–liquid extraction experiments, it has been shown that the pH-dependence of the extraction ability of malonamide derivatives depends largely on the nature of the substituents and that the effects of benzyl or *p*-methylbenzyl groups are especially large. The pH-dependence of complex formation was observed by UV/VIS spectroscopy and showed very similar behaviour to that observed in the extraction experiments. Comparison of chemical shifts in the NMR spectroscopic data for nickel(II) malonamide derivatives suggested that the aromatic ring of a benzyl group interacts with a metal ion and stabilizes the complex intramolecularly.

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