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Synthesis of a Series of Acodazole and Naphthothiophene-Deuterioporphyrins and Metalloporphyrins

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The design and synthesis of several hybrid intercalator-linked porphyrins and their corresponding metalloporphyrin derivatives designed as cellular DNA targetted anticancer agents is described. 9-Chloro-7-methylimidazo[4,5-*f*]quinoline was condensed with ethylenediamine, 1,4-phenylenediamine and 2,5-toluenediamine to give compounds **Ia**—**c**. Naphtho[2,1-*b*]thiophene-4-carboxylic acid was condensed with 1,6-hexanediamine, 1,10-decanediamine, and 1,12-dodecanediamine to give compounds **IIa**—**c** and **IIIa**—**c**. Compounds **Ia**—**c** and **IIa**—**c** were condensed with deuterioporphyrin monomethyl ester and deuterioporphyrin to yield compounds **IVa**—**j**. Compounds **IVa**—**h** were refluxed with $MnCl_2$ or $CoCl_2$ in DMF to give metalloporphyrins **Va**—**j**. Compounds **Ia**—**c**, **IIa**—**c**, **IIIa**—**c**, **IVa**—**j**, and **Va**—**j** were characterized by IR, NMR, and MS (FAB) spectral data. K_{assoc} value for intercalative binding of these porphyrin derivatives to calf thymus DNA is in the range 1.9—3.0×10^6 L M^{-1}.

Porphyrin derivatives offer several advantages in the treatment of human malignancies in terms of ready availability, good uptake properties, preferential accumulation in tumor tissue, and acceptable toxicity.[1] These properties in conjunction with the marked photosensitizing capability of the porphyrin chromophore of hematoporphyrin derivatives (HPD) has been extensively utilized in photodynamic therapy of cancer.[1] The HPD currently used clinically is, however, ill-defined chemically and therefore it is difficult to ascribe particular biochemical effects and biological responses to individual structures. In an attempt to contribute to this subject we reported the synthesis, characterization and biological evaluation of certain hemin-acridines,[2] acridine-iron porphyrins, and acodazole-iron porphyrins.[3,4] The rationale in incorporating potential DNA intercalating groups, such as 7-chloro-2-methoxy-9-acridinamine; 7-methylimidazo[4,5-*f*]quinolin-9-amine; naphtho[2,1-*b*]thiophene-4-carboxylic acid; and aminostilbene was to promote specific binding to cellular duplex DNA and thereby focus chemically characterized agents on specific cell targets.[2—4]

In addition the synthesis and characterization of the corresponding intercalator linked reducible metalloporphyrins offered the possible alternative cytotoxic mechanism of cell target directed redox-mediated DNA cleavage. In the event, the prototype hemin–spermine–acridines effected efficient, essentially sequence neutral, oxygen-mediated DNA scission in solution in the presence of a biologically compatible reducing agent, e.g. dithiothreitol or 2-mercaptoethanol, and at concentrations comparable with that employed with the iron-mediated glycopeptide and antitumor antibiotic bleomycin.[3,4] Certain of these synthetic porphyrin derivatives exhibit antibacterial activity specifically under aerobic conditions and anticancer activity against some animal and human tumor models.[4]

In this paper we report the further exploitation of these findings and the exploration of the lead structures. Specifically we report the synthesis of some deuterioporphyrin monomethyl ester[5] and deuterioporphyrin[5] condensed with 9-chloro-7-methylimidazo-[4,5-*f*]quinoline[6—8] and naphtho[2,1-*b*]thiophene-4-carboxylic acid via various diamines, together with the synthesis and characterization of the corresponding manganese and cobalt metalloporphyrin structures.

Results and Discussion

Naphtho[2,1-*b*]-thiophene-4-carboxylic acid was condensed[9] with either 1,6-hexanediamine, 1,10-decanediamine, or 1,12-dodecanediamine, using *N,N'*-carbonyldiimidazole to give *N*-(naphtho[2,1-*b*]thiophene-4-carbonyl-4-yl)-1,6-hexanediamine (**IIa**); *N*-naphtho[2,1-*b*]thiophene-4-carbonyl-4-yl)-1,10-decanediamine (**IIb**),

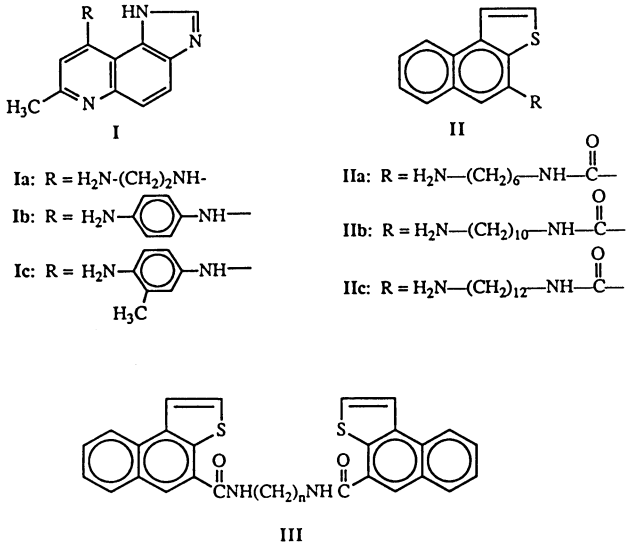


Fig. 1. Structures of the intercalating groups, acodazole (**I**) and naphtho[2,1-*b*]thiophene(**II**) used in this study together with their derivatives.

Table 1. Physical Constants and Spectral Data of Deuterioporphyrin Condensed Products (**IV**)

Sl. No.	Reaction time	Solvent of elution	Yield/%	Mp/°C	IR (ν_{max})	Mass (FAB) (m/z, rel intensity)	^{1}H NMR (δ)
IVa	20 h at R.T.	$CHCl_3$–MeOH (70 : 30)	70	210 (d)	1725 (ester), 1634 and 1625 (amide); 1600 (Ar)	(glycerol/sulfolane) 749 (2.2, M^++2); 748 (3.7, M^++1); 747 (0.7, M^+); 522 (0.2, M^+−225); 225 (6.5, $C_{13}H_{13}N_4$); 211 (6.1 $C_{13}H_{13}N_4$−CH_2); 197 (3.6, $C_{13}H_{13}N_4$−C_2H_4); 182 (3.1, $C_{11}H_8N_3$)	10.15 (m, 4H); 9.30 (m, 2H); 8.15 (m, 2H, 1H, exch.); 7.5 (d, 1H); 6.95 (m, 2H); 4.35 (m, 4H); 3.25—3.80 (m, 22H); 3.0 (m, 4H)
IVb	20 h at R.T.	$CHCl_3$–MeOH (80 : 20)	20	160 (d)	1760 (ester); 1640 (amide); 1620 (Ar)	(glycerol/sulfolane) 796 (0.5, M^++1); 795 (0.1, M^+)	10.3 (m, 4H); 9.35 (s, 2H); 8.65 (s, 1H); 8.15 (d, 1H); 7.75 (m, 4H); 7.35 (d, 2H); 7.10 (s, 2H); 6.78 (s, 1H); 4.5 (m, 4H); 3.80 (m, 18H); 3.40 (m, 4H); −4.1 (s, 1H)
IVc	48 h at R.T. and 24 h at 60 °C	$CHCl_3$–MeOH (90 : 10)	20	>300 (d)	1700 (ester); 1640 (amide); 1620 (Ar)	(glycerol/sulfolane) 810 (2.4, M^++1); 809 (1.5, M^+); 507 (0.8, M^+−302); 4.79 (2.2, M^+−330); 330 (23.6, $C_{19}H_{16}N_5O$); 302 (13.2, $C_{18}H_{16}N_5$); 120 (10.9, $C_7H_8N_2$); 119 (100, m/z 120−H)	10.25 (m, 4H); 9.30 (d, 2H); 8.6 (s, 1H); 8.10 (d, 1H); 7.8 (d, 1H); 7.40 (m, 1H); 7.10 (bs, 2H); 6.72 (s, 1H); 4.3 (m, 4H); 3.40 (m, 19H); 1.8 (d, 3H). One methyl may be under DMSO-d_6 peak at 2.50.
IVd	48 h at 55 °C and 40 h at R.T.	$CHCl_3$–MeOH (98 : 2)	37	190 (d)	3300 (–NH–); 1730 (ester); 1635 (amide)	(glycerol/sulfolane) 833 (1.7, M^++1); 832 (0.5, M^+); 507 (0.8, M^+−325); 353 (2.3, $C_{20}H_{21}N_2SO_2$); 325 (0.1, $C_{19}H_{21}N_2SO$); 226 (4.0, $C_{13}H_8NSO$); 211 (11.6, $C_{13}H_7SO$); 183 (7.6, $C_{12}H_7S$)	10.3 (s, 1H); 10.15 (t, 3H); 9.20 (d, 2H); 8.55 (d, 1H); 8.35 (m, 1H); 8.20 (m, 1H); 8.0 (m, 2H); 7.72 (m, 3H); 4.35 (m, 4H); 3.70 (m, 15H); 3.35 (m, 4H); 3.0 (m, 4H); 1.2 (m, 8H)
IVe	48 h at 55 °C and 40 h at R.T.	$CHCl_3$–MeOH (98 : 2)	46	170 (d)	3290 (–NH–); 1730 (ester); 1635 (amide)	(glycerol/DMF/solfolane) 951 (0.1, M^++Cu); 211 (3.3, $C_{13}H_7SO$); 183 (5.1, $C_{12}H_7S$). This compound picks up Cu from the Cu probe.	10.2 (m, 4H); 9.25 (d, 2H); 8.85 (m, 1H); 8.55 (d, 1H); 8.45 (s, 1H), 8.25 (dd, 1H); 8.10 (d, 1H); 8.02 (d, 1H); 7.7 (m, 3H); 4.40 (m, 4H); 3.7 (m, 15H); 3.35 (m, 4H); 3.0 (m, 4H); 1.2 (m, 16H)
IVf	48 h at 55 °C and 40 h at R.T.	$CHCl_3$–MeOH (98 : 2)	50	135 (d)	3300 (–NH–); 1730 (ester); 1630 (amide)	(DMF/sulfolane) 917 (33.6, M^++1); 916 (6.7, M^+); 705 (1.4, M^+−$C_{13}H_7SO$); 211 (21.6, $C_{13}H_7SO$); 183 (18.9, $C_{12}H_7S$)	10.2 (m, 4H); 9.2 (m, 2H); 8.85 (m, 1H, exch.); 8.55 (d, 1H); 8.45 (s, 1H); 8.20 (m, 1H); 8.06 (d, 1H); 7.95 (d, 1H); 7.7 (m, 3H); 4.35 (m, 4H); 3.7 (m, 15H); 2.95 (m, 4H); 1.2 (m, 24H)

Table 1. (Continued)

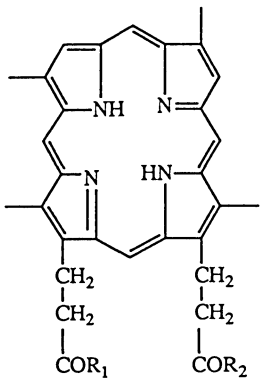
Sl. No.	Reaction time	Solvent of elution	Yield/%	Mp/°C	IR (ν_{max})	Mass (FAB) (m/z, rel intensity)	^{1}H NMR (δ)
IVg	20 h at R.T.	$CHCl_3$–MeOH (70 : 30)	25	280 (d)	3300 (–NH–); 1640 and 1620 (amide); 1600 (Ar)	(glycerol/sulfolane) 958 (1.7, M^++2); 957 (2.1, M^++1), 956 (0.3, M^+); 716 (0.2, $M^+-C_{13}H_{14}N_5$); 660 (0.4, $M^+-C_{16}H_{18}N_5O$); 476 (1.9, 716$-C_{13}H_{14}N_5$); 364 (5.8, 660$-C_{16}H_{18}N_5O$); 296 (11.7, $C_{16}H_{18}N_5O$); 240 (17.3, $C_{13}H_{14}N_5$); 183 (31.7, $C_{11}H_9N_3$); 182 (83.7, $C_{11}H_8N_3$); 168 (100, $C_{11}H_8N_3-CH_3$)	10.25 (d, 2H); 10.10 (d, 2H); 9.30 (m, 3H, 1H exch.); 8.54 (m, 2H); 8.30 (d, 2H); 7.65 (q, 2H); 7.3 (t, 2H); 6.22 (d, 2H); 4.3 (m, 4H); 3.60 (m, 13H); 3.10 (m, 9H); 1.9 (d, 6H)
IVh	48 h at 55 °C and 40 h at R.T.	$CHCl_3$–MeOH (98 : 2)	15	232 (d)	3300 (–NH–); 1635 (amide)	(glycerol/DMF/sulfolane) 1127 (1.1, M^++1); 1126 (0.8, M^+); 381 (6.2, $C_{22}H_{25}N_2O_2S$); 353 (6.6, $C_{20}H_{21}N_2O_2S$); 325 (5.4, $C_{19}H_{21}N_2OS$); 310 (5.0, $C_{19}H_{20}NOS$); 226 (5.3, $C_{13}H_8NOS$); 211 (12.4, $C_{13}H_7OS$); 183 (6.9, $C_{12}H_7S$)	10.15 (m, 4H); 9.16 (d, 2H); 8.75 (m, 2H); 8.5 (d, 2H); 8.35 (d, 2H); 8.20 (d, 2H); 8.05 (d, 2H); 7.95 (d, 2H); 7.65 (m, 4H); 4.35 (m, 4H); 3.65 (q, 12H); 3.1 (m, 12H); 1.25 (m, 16H)
IVi	40 h at 50 °C and 40 h at R.T.	$CHCl_3$–MeOH (98 : 2)	9	220 (d)	3300 (–NH–); 1635 (amide)	(DMF/Cleland's reagent) 1239 (8.1, M^++1); 1238 (2.1, M^+); 409 (10.6, $C_{24}H_{29}N_2O_2S$); 211 (55.2, $C_{13}H_7SO$); 183 (20.0, $C_{12}H_7S$); 140 (3, $C_{10}H_{20}$)	10.3 (m, 4H); 9.3 (m, 2H); 8.84 (m, 2H); 8.55 (m, 2H); 8.44 (m, 2H); 8.23 (m, 2H); 8.05 (m, 2H); 7.90 (m, 4H); 7.7 (m, 4H); 4.35 (m, 4H); 3.70 (m, 2H); 2.85 (m, 4H); 2.05 (m, 4H); 0.8 (m, 36H)
IVj	20 h at R.T.	$CHCl_3$–MeOH (98 : 2)	7	195	3300 (–NH–); 1635 (amide)	(DMF/Cleland's reagent) 1295 (2.2, M^++1); 1294 (3.0, M^+); 1293 (3.0, M^+-1); 465 (1.3, $C_{28}H_{37}N_2O_2S$); 226 (2.4, $C_{13}H_8NSO$); 211 (84.6, $C_{13}H_7SO$); 183 (22.6, $C_{12}H_7S$)	10.3 (m, 4H); 9.3 (d, 2H); 8.86 (m, 2H); 8.55 (d, 2H); 8.45 (s, 2H); 8.25 (d, 2H); 8.05 (d, 2H); 7.95 (m, 4H); 7.7 (m, 4H); 4.35 (m, 4H); 3.70 (q, 12H); 3.05 (m, 4H); 2.85 (m, 2H); 0.8 (m, 44H)

All ^{1}H NMR spectra were run in DMSO-d_6.

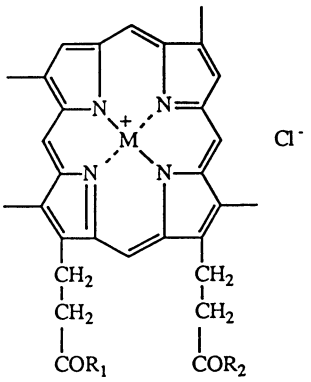
and *N*-(naphtho[2,1-*b*]thiophene-4-carbonyl-4-yl)-1,12-dodecanediamine (**IIc**) respectively (Fig. 1). During these condensation reactions compounds **IIIa**—**c** (Fig. 1) were also isolated as minor products.

Deuterioporphyrin was prepared from hemin by the method of Caughey et al.[5] Deuterioporphyrin monomethyl ester was prepared by the controlled hydrolysis of deuterioporphyrin with 4 M hydrochloric acid and chromatographic separation of the resulting mixture of mono- and dicarboxylic acids followed by conventional esterification.[2-4,5]

Condensation of the functionalized chromophores bearing the amine linkers **Ia**—**c** and **IIa**—**c** (Fig. 1) with either deuterioporphyrin monomethyl ester or deuterioporphyrin in the presence of *N,N'*-carbonyldiimidazole and *N*-methylmorpholine following previously described procedures[2,4] afforded compounds **IVa**—**j** (Fig. 2). The composition and structures of the products were confirmed by analytical and spectroscopic procedures summarized in Table 1. These hybrid porphyrin-linked intercalators, comprising derivatives of both deuterioporphyrin monomethyl ester and deuterioporphyrins, (**IVa**—**g**, Fig. 2) were then converted to the corresponding metalloporphyrins (**V**, Fig. 3) by heating with $CoCl_2$ or $MnCl_2$ in DMF. Again the composition and structures of **Va**—**j** were confirmed by spectroscopic and analytical data which are given in Table 1. The intercalator-porphyrin hybrids bind to double stranded calf thymus DNA with K_{assoc} values determined at pH 7.0 and 37 °C in the range 1.9 to 3.0×10^6 L M^{-1}, while neither the porphyrin nor metalloporphyrin components lacking the DNA interactive moieties bind to



IV



V

IVa: $R_1 = OCH_3$; $R_2 = -NH-(CH_2)_2-NH-I$

IVb: $R_1 = OCH_3$; $R_2 = -NH-C_6H_4-NH-I$

IVc: $R_1 = OCH_3$; $R_2 = -NH-C_6H_3(CH_3)-NH-I$

IVd: $R_1 = OCH_3$; $R_2 = -NH-(CH_2)_6-NH-C(=O)-II$

IVe: $R_1 = OCH_3$; $R_2 = -NH-(CH_2)_{10}-NH-C(=O)-II$

IVf: $R_1 = OCH_3$; $R_2 = -NH-(CH_2)_{12}-NH-C(=O)-II$

IVg: $R_1 = R_2 = -NH-(CH_2)_2-NH-I$

IVh: $R_1 = R_2 = -NH-(CH_2)_6-NH-C(=O)-II$

IVi: $R_1 = R_2 = -NH-(CH_2)_{10}-NH-C(=O)-II$

IVj: $R_1 = R_2 = -NH-(CH_2)_{12}-NH-C(=O)-II$

Fig. 2. Structures of synthetic hybrid intercalator-deuterioporphyrins.

Va: $R_1 = OCH_3$; $R_2 = -NH-(CH_2)_2-NH-I$; M = Mn

Vb: $R_1 = OCH_3$; $R_2 = -NH-C_6H_4-NH-I$; M = Mn

Vc: $R_1 = OCH_3$; $R_2 = -NH-(CH_2)_2-NH-I$; Mn = Co

Vd: $R_1 = OCH_3$; $R_2 = -NH-C_6H_4-NH-I$; M = Co

Ve: $R_1 = OCH_3$; $R_2 = -NH-C_6H_3(CH_3)-NH-I$; M = Co

Vf: $R_1 = OCH_3$; $R_2 = -NH-(CH_2)_6-NH-C(=O)-II$; M = Mn

Vg: $R_1 = OCH_3$; $R_2 = -NH-(CH_2)_{10}-NH-C(=O)-II$; M = Mn

Vh: $R_1 = OCH_3$; $R_2 = -NH-(CH_2)_{12}-NH-C(=O)-II$; M = Mn

Vi: $R_1 = R_2 = -NH-(CH_2)_2-NH-I$; M = Mn

Vj: $R_1 = R_2 = -NH-(CH_2)_2-NH-I$; M = Co

Fig. 3. Structures of synthetic hybrid intercalator-metalloporphyrins.

DNA under these conditions.[3,4]

Thus, although it is recognized that other pharmacological factors including cellular uptake must be taken into account, the effective binding to DNA of the intercalative moiety may well to be an important contributor to the expression of anticancer properties in these novel structures.

The anticancer cytotoxic and cytostatic properties of these new agents will be reported in due course.

Experimental

Melting points were determined on a Fisher-Johns apparatus and are uncorrected. Only the principal sharply defined IR peaks are reported. ^{1}H NMR spectra were recorded on approximately 5—15% (w/v) solutions in appropriate deuterated solvents with tetramethylsilane as internal standard. Line positions are recorded in ppm from the reference. The MS spectrometer peak measurements were made by comparison with perfluorotributylamine at a resolving power of 15000.

Condensation of 9-Chloro-7-methylimidazo[4,5-*f*]quinoline with Ethylenediamine (I). 9-Chloro-7-methylimidazo[4,5-*f*]-quinoline (2.17 g, 0.01 mol) and ethylenediamine (1.2 g, 0.02 mol) in absolute ethanol (30 mL) was stirred under reflux overnight. The reaction contents were concentrated in vacuo and the crude solid obtained was recrystallized from ethanol to give (2-aminoethylamino)acodazole (**Ia**, Fig. 1), 1.4 g (55% yield). mp 250 °C; IR (Nujol) ν_{max} 3425 and 3300 (-NH_2 and -NH-), 1615 and 1605 (Ar) cm^{-1}; ^{1}H NMR (D_2O) δ=7.9 (s, 1H, Ar), 7.25 (d, 1H, Ar), 6.60 (d, 1H, Ar), 5.80 (d, 1H, Ar), 3.15 (t, 2H, -CH_2-); 2.88 (t, 2H, -CH_2-), 2.15 (s, 3H, -CH_3). MS *m/z* (rel intensity): 242.1353 (1.97, M^++1); 241.1329 (13.31, M^+); (Calcd for $C_{13}H_{15}N_5$: M, 241.1328); 211.0985 [100, M^+—(CH_2NH_2)]; 182.0710 [2.52, M^+—(NH_2CH_2-NH-)].

Similarly, condensation of 9-chloro-7-methylimidazo[4,5-*f*]-quinoline with 1,4-phenylenediamine and 2,5-toluenediamine gave 9-(4-aminoanilino)-7-methylimidazo[4,5-*f*]quinoline (**Ib**, Fig. 1). Yield, m.p. and spectral data of **Ib** and **Ic** are reported below.

Ib: Yield 70%; mp 300 (decomp). IR (Nujol) ν_{max} 3250 (b, -NH_2 and -NH-), 1610 (Ar) cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=10.44 (s, 1H, exch), 8.46 (s, 1H, Ar), 7.88 (d, 1H, Ar), 7.65 (d, 1H, Ar), 7.10 (d, 2H, Ar), 6.70 (t, 3H, Ar), 5.14 (bs, 1H, exch.), 2.44 (s, 3H, -CH_3). MS *m/z* (rel intensity): 290.1354 (19.78, M^++1); 289.1324 (100, M^+); (Calcd for $C_{17}H_{17}N_5$: M, 289.1324); 288.1299 (19.30, M^+—H).

Ic: Yield 75%; mp 275 (decomp). IR (Nujol) ν_{max} 3400—3000 (b, -NH_2 and -NH-), 1610 (Ar) cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=10.35 (s, 1H, exch), 8.45 (s, 1H, Ar), 7.85 (d, 1H, Ar), 7.60 (d, 1H, exch), 6.98 (m, 2H, Ar), 6.70 (m, 1H, Ar), 6.60 (s, 1H, Ar), 4.85 (bs, 2H, exch), 2.40 (s, 3H, -CH_3), 2.10 (s, 3H, -CH_3). MS *m/z* (rel intensity) 304.1517 (21.66, M^++1); 303.1487 (100, M^+); (Calcd for $C_{18}H_{17}N_5$: M, 303.1486); 302.1396 (10.40, M^+—H); 288.1239 (3.10, M^+—CH_3).

Condensation of Naphtho[2,1-*b*]thiophene-4-carboxylic Acid with 1,6-Hexanediamine (II and III). Naphtho[2,1-*b*]thiophene-4-carboxylic acid (228 mg, 1 mmol) and *N,N'*-carbonyldiimidazole (243 mg, 1.5 mmol) were taken up in 8 mL dry THF and the reaction contents were stirred for 6 h at room temperature. 1,6-Hexanediamine (1.16 g, 10 mmol) was added to the reaction mixture and stirred at room temperature for 48 h and at 50 °C for 40 h. The solvent was removed in vacuo and the residue was washed thoroughly with water and subjected to column chromatography over silica gel. Elution with $CHCl_3$–ethyl acetate (90 : 10) gave **IIIa** (Fig. 1), yield 50 mg (9%), mp 230 °C. IR (Nujol) ν_{max} 3340 and 3300 (-NH-), 1670 and 1625 (amide) cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=8.9 (t, 2H), 8.5 (q, 4H), 8.25(d, 2H), 8.1 (d, 2H), 8.0 (d, 2H), 7.7 (m, 4H), 3.4 (q, 4H), 1.6 (m, 8H). MS *m/z* (rel intensity) 535.1591 (39.69, M^+); (Calcd for $C_{32}H_{28}N_2O_2S_2$: M, 536.1593); 325.137 (5.23, $C_{19}H_{21}N_2SO$); 308.1110 (20.82, $C_{19}H_{18}NSO$); 296.1110 (18.62, $C_{18}H_{18}NSO$); 211.0219 (100, $C_{13}H_7SO$); 183.0263 (56.46, $C_{12}H_7S$).

Further elution of the column with $CHCl_3$–MeOH (75 : 25) gave some impurity and then further elution with MeOH gave product **IIa**. 150 mg (46% yield), mp 155 °C. IR (Nujol) ν_{max} 3350 and 3300 (-NH_2-), 3200 (-NH-), 1630 (amide) cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=8.95 (t, 1H, exch), 8.55 (t, 2H), 8.25 (d, 1H), 8.10 (d, 1H), 8.0 (d, 1H), 7.7 (m, 2H), 3.35 (t, after D_2O exch, 2H), 1.40 (m, 10H). MS *m/z* (rel intensity) 326.1447 (30.74; M^+); (Calcd for $C_{19}H_{22}N_2SO$: 326.1453); 297 (36.59, $C_{18}H_{19}NSO$); 211.0218 (100, $C_{13}H_7SO$); 183.0261 (70.90, $C_{12}H_7S$).

Similarly prepared were **IIb**, **IIIb**, and **IIc** and **IIIc** and their yields, mp's and solvent of elution are given below.

IIb: Yield 65%; mp 90 °C; solvent of elution $CHCl_3$–MeOH (75 : 25). IR (Nujol) ν_{max} 3300 (-NH_2, -NH-), 1670 and 1630 (amide) cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=8.9 (bs, 1H, exch), 8.60 (d, 1H, Ar), 8.45 (s, 1H, Ar), 8.25 (d, 1H, Ar), 8.10 (d, 1H, Ar), 8.0 (d, 1H, Ar), 7.70 (m, 2H, Ar), 3.4 (t, 2H), 1.4 (m, 18H). CIMS *m/z* (rel intensity) 383 (100, M^++1), 356 (1.6, M^+—NH_2).

IIIb: Yield 17%; mp 200 °C; solvent of elution $CHCl_3$–MeOH (75 : 25). IR (Nujol) ν_{max} 3280 (-NH-), 1630 (amide) cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=8.90 (t, 2H), 8.70 (d, 2H), 8.46 (s, 2H), 8.26 (d, 2H), 8.10 (d, 2H), 8.0 (d, 2H), 7.7 (m, 4H), 3.3 (m, 4H, after D_2O exch), 1.55 (m, 16H). CIMS *m/z* (rel intensity) 593 (45.2, M^+ +1), 409 (21.3, M^+—$C_{12}H_7S$), 381 (6.1, *m/z* 409—CO), 366 (8.2, *m/z* 381—NH), 352 (12.0, *m/z* 366—CH_2).

IIc: Yield 36%; mp 108 °C; solvent of elution $CHCl_3$–MeOH (80 : 20). IR (Nujol) ν_{max} 3330—3280 (-NH_2 and -NH-), 1650 (amide) cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=8.90 (t, 1H, -NH-, exch), 8.60 (d, 1H, Ar), 8.48 (s, 1H, Ar), 8.25 (d, 1H, Ar), 8.10 (d. 1H, Ar), 8.0 (d, 1H, Ar), 7.70 (m, 2H, Ar), 3.40 (t, 2H), 1.40 (m, 22H). CIMS *m/z* (rel intensity) 411 (100, M^++1).

IIIc: Yield 26%; mp 160 °C; solvent of elution $CHCl_3$–MeOH (75 : 25). IR (Nujol) ν_{max}: 3300 (-NH-), 1670 and 1630 (amide) cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=8.90 (t, 2H), 8.55 (d, 2H), 8.45 (s, 2H), 8.25 (dd, 2H), 8.10 (d, 2H), 8.0 (d, 2H), 7.7 (m, 4H), 3.3 (m, 4H; after D_2O exchange), 1.4 (m, 20H). CIMS *m/z* (rel intensity) 621 (22.2, M^++1); 437 (12.1, M^+—$C_{12}H_7S$); 409 (5.0, *m/z* 437—CO); 394 (4.5, *m/z* 409—NH).

Condensation of Deuterioporphyrin Monomethyl Ester with (2-Aminoethylamino)acodazole to Give IVa. Deuterioporphyrin monomethyl ester (524 mg, 1 mmol) was taken up in 20 mL dry DMF and to it was added *N,N'*-carbonyldiimidazole (243 mg, 1.5 mmol) and the reaction contents were stirred for 6 h at room temperature and then (2-aminoethylamino)acodazole (**Ia**) 482 mg, 2 mmol) was added. The reaction mixture was stirred at room temperature for 20 h.

The solvent was removed in vacuo and the residue was subjected to column chromatography. Elution with $CHCl_3$–MeOH (70 : 30) gave **IVa**. Similarly **11b**, **IIIc**, and **IIIa—c** were each condensed with deuterioporphyrin monomethyl ester to give **IVb—IVf**. Reaction time, solvent of elution, mp, yield, and spectral data of these compounds (**IVa—j**) are reported in Table 1.

Condensation of Deuterioporphyrin with (2-Aminoethylamino)acodazole to Give IVg. Deuterioporphyrin (128 mg, 0.25 mmol) and *N,N'*-carbonyldiimidazole (122 mg, 0.75 mmol) was taken in dry DMF (10 mL) and stirred at room temperature for 6 h and then (2-aminoethylamino)acodazole (**Ia**) (180 mg, 0.75 mmol) was added. The reaction mixture was stirred at room temperature for 20 h, the solvent was then removed under reduced pressure and the residue was subjected to column chromatography. Elution with $CHCl_3$–MeOH (70 : 30) gave **IVg**. Similarly deuterioporphyrin was condensed with **IIIa—c** to give **IVh—j** (Fig. 2). Reaction time, solvent of elution, yield, mp, and spectral data of **IVg—j** are reported in Table 1.

Preparation of Metalloporphyrins Va—j. A solution of deuterioporphyrin monomethyl ester (**IVa**) (75 mg, 0.1 mmol) and $MnCl_2 \cdot 4H_2O$ (80 mg, 0.4 mmol) in DMF was refluxed for 1 h and then the solvent was removed under reduced pressure and the residue was subjected to column chromatography over silica using $CHCl_3$–MeOH (80 : 20) as eluent to give compound **Va**. Similarly prepared were the other compounds **Vb—j** (Fig. 2). Reaction time, solvent of elution, yield, mp, and

Table 2. Physical Constants and Spectral Data of Metalloporphyrins (V)

Sl. No.	Reaction time	Solvent of elution	Yield/%	Mp/°C	IR (ν_{max})	Mass (FAB) (m/z, rel intensity)
Va	1 h at 125 °C	$CHCl_3$–MeOH (80 : 20)	56	>300	1725 (ester); 1635 and 1620 (amide); 1595 (Ar)	801 (15.6, M^++1); 800 (12.5, M^+) 225 (11.7, $C_{13}H_{13}N_4$); 211 (15.7, $C_{12}H_{11}N_4$); 197 (5.4, $C_{11}H_9N_4$)
Vb	1 h at 125 °C	$CHCl_3$–MeOH (80 : 20)	58	270 (d)	1725 (ester); 1634 and 1620 (amide); 1590 (Ar)	849 (5.2, M^++1); 848 (8.8, M^+); 504 (1.4, M^+−344); 344 (2.4, $C_{20}H_{18}NO$); 316 (501, $C_{18}H_{14}N_5O$); 288 (207, $C_{17}H_{14}N_5$); 197 (4.9, $C_{11}H_9N_4$)
Vc	1 h at 125 °C	$CHCl_3$–MeOH (80 : 20)	50	>300 (d)	1720 (ester); 1600 (Ar)	805 (0.5, M^++1); 804 (0.1, M^+); 197 (1.4, $C_{11}H_9N_4$)
Vd	1 h at 125 °C	$CHCl_3$–MeOH (80 : 20)	50	300 (d)	1730 (ester); 1660 (amide); 1620 (–CH= N–); 1605 and 1590 (Ar)	853 (0.4, M^++1); 852 (0.1, M^+); 316 (2.1, $C_{18}H_{14}N_5O$)
Ve	0.5 h at 125 °C	$CHCl_3$–MeOH (80 : 20)	70	>300	1720 (ester); 1650 and 1630 (amide); 1595 (Ar)	867 (0.1, M^++1); 866 (0.1, M^+); 288 (1.9, $C_{17}H_{14}N_5$); 273 (2.75, $C_{17}H_{13}N_4$); 197 (2.8, $C_{11}H_9N_4$)
Vf	1 h at 125 °C	$CHCl_3$–MeOH (95 : 5)	24	162 (d)	3300 (–NH–); 1730 (ester); 1645 (amide)	886 (2.3, M^++1); 885 (4.2, M^+); 884 (5.7, M^+−1); 211 (3.9, $C_{13}H_7SO$); 183 (4.6, $C_{12}H_7S$)
Vg	1 h at 125 °C	$CHCl_3$–MeOH (95 : 5)	30	160 (d)	1733 (ester); 1652, 1646 and 1636 (amide); 1615 (Ar)	942 (1.7, M^++1); 941 (2.1, M^+); 241 (51.8, $C_{14}H_{11}NSO$)
Vh	1 h at 125 °C	$CHCl_3$–MeOH (95 : 5)	17	155 (d)	3300 (–NH–); 1730 (ester); 1635 (amide); 1535 (Ar)	970 (2.4, M^++1); 969 (0.3, M^+); 211 (2.4, $C_{13}H_7SO$); 183 (3.7, $C_{12}H_7S$)
Vi	1 h at 125 °C	$CHCl_3$–MeOH (80 : 20)	70	>300 (d)	3350 (–NH–); 1650 (amide)	1010 (2.5, M^++1); 1009 (1.5, M^+); 225 (18.9, $C_{13}H_{13}N_4$); 197 (9.4, $C_{11}H_9N_4$); 182 (13.3, $C_{11}H_8N_3$)
Vj	0.5 h at 125 °C	$CHCl_3$–MeOH (80 : 20)	13	>300 (d)	1635 (amide); 1610 (Ar)	1015 (3.0, M^++2); 1014 (4.4, M^++1); 1013 (1.0, M^+); 296 (5.5, $C_{16}H_{18}N_5O$); 268 (14.1, $C_{14}H_{14}N_5O$); 240 (13.0, $C_{13}H_{14}N_5$); 225 (41.4, $C_{13}H_{13}N_4$); 211 (52.7, $C_{12}H_{11}N_4$).

Compounds **Vi** and **Vj** were eluted on neutral Al_2O_3 column. IR Spectra of **Vc** and **Vg** were run using MeOH cast. All other compounds were run using Nujol. FAB mass was run using sulfolane/glycerol.

spectral data of **Va**—**j** are reported in Table 2.

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