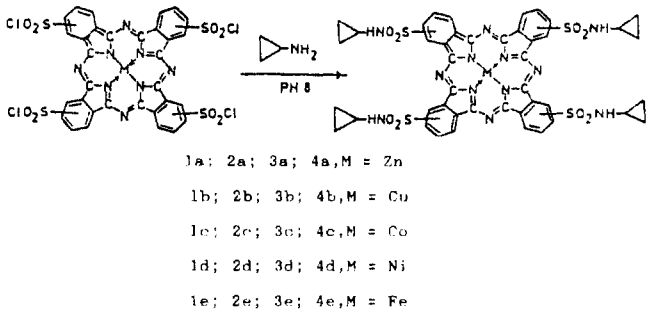
Scheme I



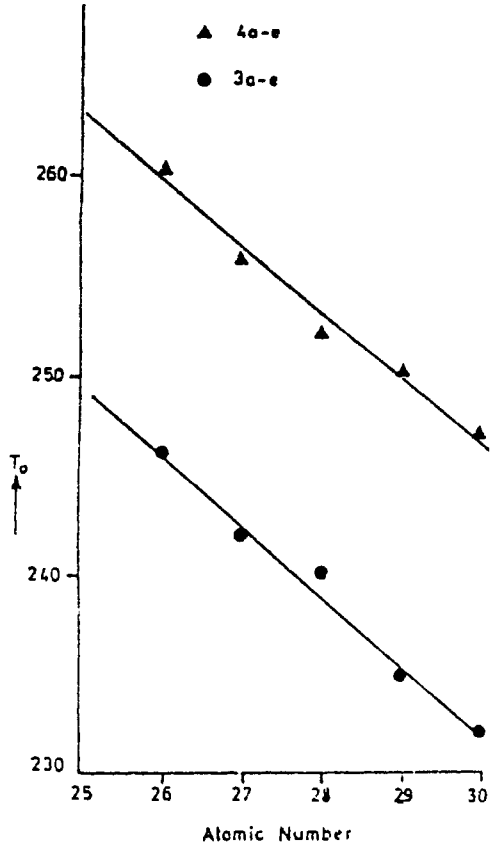


Figure 1. Relationship between pyrolytic cyclopropyl ring opening temperatures and metal atomic numbers for compounds **3a–e** and **4a–e**.

heated to 45–47 °C for 3 h. During this reaction the pH was kept constant at 8 by adding 2 N NH_4OH. The solution was then acidified with 10% HCl (60 ml) and left to stand for 1 h at room temperature. The precipitate was filtered off, washed with water, and then dried under vacuum to yield **3a–e**. IR (KBr) 3200–3300 (NH); 1030–1040, 1440–1460 (cyclopropyl); 1155–1160, 1320–1330 (C–SO_2–N); 890–930 (S–N) and 385–400 (M–N) cm^{-1}. Yields, ^1H NMR data, and DTA results are given in Table I. Figure 1 shows the relationship between cyclopropyl ring opening temperature (T_0) and the atomic number of the corresponding metal.

Table I. Yields and Physical Properties of the Compounds Prepared

compd	yield, %	^1H NMR (DMSO-d_6) δ 4 $(CH_2)_2$	4 CH	4 NH[a]	12 H_{arom}	cyclopropyl ring opening temp, T_0, °C
3a	70	0.668 (m)	2.43 (m)	4.46	8.12 (m)	232
3b	80	0.70 (m)	2.48 (m)	4.40	8.11 (m)	235
3c	65	0.54 (m)	2.51 (m)	4.36	8.18 (m)	240
3d	60	0.70 (m)	2.52 (m)	4.20	8.07 (m)	242
3e	75	0.51 (m)	2.48 (m)	3.54	8.06 (m)	246
4a	80	0.42 (m)	2.35 (m)	4.32	7.58 (m)	247
4b	66	0.54 (m)	2.42 (m)	3.97	7.39 (m)	250
4c	78	0.47 (m)	2.43 (m)	3.58	8.05 (m)	252
4d	64	0.55 (m)	2.35 (m)	3.99	7.90 (m)	256
4e	70	0.43 (m)	2.42 (m)	3.36	7.99 (m)	260

[a] Broad signals assigned for NH protons.

Compounds **4a–e** was prepared starting with **2a–e** in a similar manner as described above for compounds **3a–e**.

Metal Phthalocyanine-4,4′,4″,4‴-tetrakis(N-cyclopropylsulfonamides) (4a–e). IR (KBr) 3250–3400 (NH); 1035–1040, 1450–1480 (cyclopropyl); 1160–1165, 1330–1335 (C–SO_2–N); 910–950 (S–N) and 400–420 (M–N) cm^{-1}. Yields and ^1H NMR data are reported in Table I. DTA data are given in Table I and Figure 1.

Registry No. **1a**, 114251-83-1; **1b**, 14518-21-9; **1c**, 114251-84-2; **1d**, 14325-19-0; **1e**, 114251-85-3; **2a**, 114251-86-4; **2b**, 28802-09-7; **2c**, 107011-09-6; **2d**, 105766-71-0; **2e**, 114251-87-5; **3a**, 114251-88-6; **3b**, 114251-89-7; **3c**, 114251-90-0; **3d**, 114251-91-1; **3e**, 114251-92-2; **4a**, 114251-93-3; **4b**, 114251-94-4; **4c**, 114251-95-5; **4d**, 114251-96-6; **4e**, 114251-97-7; cyclopropylamine, 765-30-0; phthalocyanine-3,3′,3″,3‴-tetrakis(sulfonyl chloride), 114273-29-9; phthalocyanine-4,4′,4″,4‴-tetrakis(sulfonyl chloride), 75922-27-9.

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Synthesis of 4-Aminopyrimido[4′,5′:4,5]thieno[2,3-*b*]quinolines

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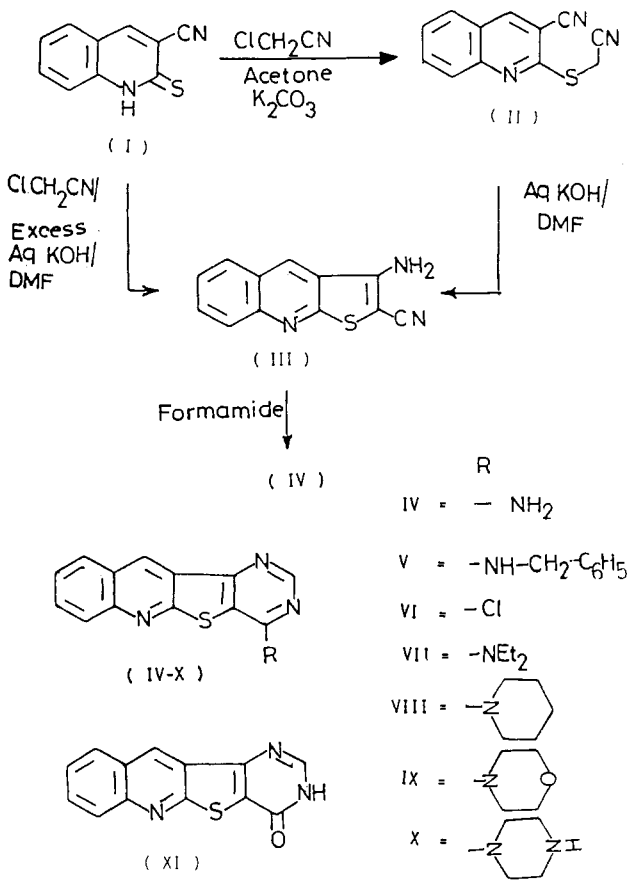
Compounds containing 4-aminothieno[3,2-*d*]pyrimidine in a novel tetracyclic condensed quinoline system are synthesized for evaluating their blood platelet aggregation inhibition activity.

A number of 4-aminothieno[3,2-*d*]pyrimidines have been found to exhibit blood platelet aggregation inhibition activity (*1–3*). We report herein the synthesis of 4-aminopyrimido-[4′,5′:4,5]thieno[2,3-*b*]quinoline (IV) and its derivatives (V, VII–X) which contain the thieno[3,2-*d*]pyrimidine structure in

0021-9568/88/1733-0530$01.50/0

Scheme I



a condensed quinoline system for evaluating their blood platelet aggregation inhibition activity.

The method employed for the synthesis of compound IV is analogous to that reported by us for synthesizing compound XI (*4*). N-substituted derivatives were prepared by reacting various amines with compound VI which was in turn obtained by the action of phosphorus oxychloride on compound XI (Scheme I).

All compounds gave satisfactory elemental analysis (C, H, N). The IR spectra of compounds II and III showed the required number of bands in the region of 2230–2300 cm^{-1} (C≡N). Compounds III, IV, V, and X showed characteristic -NH- stretching frequency bands in the region of 3050–3400 cm^{-1}. Table I summarizes the characterization data of all compounds.

Experimental Section

All melting points are uncorrected. Infrared spectra were recorded on a Perkin Elmer Model 1780 infrared spectrometer. ^1H NMR spectra were recorded on a Hitachi-R 600, a Varian T-60, or a Brucker-90 spectrometer. Mass spectra were recorded on a Jeol-D 300 spectrometer.

2-Cyanomethylthioquinoline-3-carbonitrile (II). A mixture of 3-cyanoquinoline-2(1*H*)-thione (1.0 g) in acetone (100 mL), anhydrous potassium carbonate (2.0 g), and chloroacetonitrile (1 mL) was heated under reflux for 5 h. The reaction mixture was cooled, filtered, and washed with dry acetone. Combined filtrate was evaporated to obtain crude product. It was purified by passing through a column of alumina in benzene and recrystallized from benzene–petroleum ether into yellow needles.

2-Cyano-3-aminothieno[2,3-b]quinoline (III). To a solution of II (0.5 g) in dimethylformamide (5 mL) was added with stirring aqueous potassium hydroxide (10%, 5 mL). After 30 min water (10 mL) was added to the reaction mixture and the product was collected by filtration. It was recrystallized from excess of acetonitrile into reddish-yellow needles.

This compound was also obtained from compound I (0.5 g) by using aqueous potassium hydroxide (10%, 10 mL).

4-Aminopyrimido[4′,5′:4,5]thieno[2,3-b]quinoline (IV). A solution of III (1.0 g) in formamide (20 mL) was heated under reflux for 3 h. The reaction mixture was cooled and poured into cold water. The product was collected by filtration and recrystallized from acetic acid into pale yellow needles.

4-Chloropyrimido[4′,5′:4,5]thieno[2,3-b]quinoline (VI). A mixture of compound XI (1.0 g) and phosphorus oxychloride (30 mL) was heated under reflux for 8 h. After distilling off phosphorus oxychloride (20 mL) under reduced pressure the reaction mixture was poured onto crushed ice. The product was collected by filtration and recrystallized from acetonitrile into silky needles.

General Method for the Condensation of Amines with VI. To a solution of compound VI (0.5 g) in dimethylformamide (10 mL) was added anhydrous potassium carbonate (0.5 g) and amine (0.5 g). The reaction mixture was heated under reflux for 3 h. The cold reaction mixture was then poured onto ice-cold water. The product was filtered and recrystallized from a suitable solvent.

Table I. Characterization Data of Compounds

compd	mp, °C (% yield)	^1H NMR δ; mass *m/e* (% abundance)
II	305 (90)	$CDCl_3$: 3.6 (2 H, s, S-CH_2), 7.4–8 (4 H, m, H-5, -6, -7, -8), 8.4 (1 H, s, H-4)
III	295 (80)	DMSO-d_6: 7.5 (2 H, bs, -NH_2), 7.6–8.2 (4 H, m, H-5, -6, -7, -8), 9.1 (1 H, s, H-4)
IV	>340 (80)	CF_3COOH: 8.1–8.8 (4 H, m, H-7, -8, -9, -10) 9.1 (1 H, s, H-11), 10.2 (1 H, s, H-2); mass 252 (M^+, 100), 226 (6.5), 225 (40.6), 198 (6.15), 154 (13.6), 153 (9), 126 (10)
V	265 (60)	CF_3COOH: 5.2 (2 H, s, -CH_2), 7.5 (5 H, s, Ar-H), 8.2–8.7 (4 H, m, H-7, -8, -9, -10), 9.1 (1 H, s, H-2) 10.1 (1 H, s, H-2)
VI	230 (63)	$CDCl_3$: 7.3–8.2 (4 H, m, H-7, -8, -9, -10), 9.1 (1 H, s, H-11), 9.3 (1 H, s, H-2)
VII	140 (90)	$CDCl_3$: 1.2–1.5 (6 H, t, 2-CH_3), 3.6–4 (4 H, q, 2CH_2), 7.2–8.2 (4 H, m, H-7, -8, -9, -10), 8.2 (1 H, s, H-11), 9.1 (1 H, s, H-2)
VIII	160 (67)	$CDCl_3$: 1.7 (6 H, bs, -3CH_2), 3.9 (4 H, bs, -2NCH_2), 7.3–8.1 (4 H, m, H-7, -8, -9, -10), 8.65 (1 H, s, H-11), 9 (1 H, s, 2-H); mass: 320 (M^+, 100), 291 (24.5), 265 (12.7) 264 (15), 252 (20.5), 237 (4.8)
IX	204 (75)	$CDCl_3$: 4 (8 H, bs, -CH_2), 7.3–8.2 (4 H, m, H-7, -8, -9, -10), 8.75 (1 H, s, H-11), 9.2 (1 H, s, H-2); mass: 322 (M^+, 100), 321 (17), 292 (14), 291 (39), 278 (12), 277 (40), 266 (18), 265 (78), 264 (47), 237 (44), 210 (41)
X	190 (58)	

Registry No. I, 69513-35-5; II, 115913-33-2; III, 115913-34-3; IV, 115913-35-4; V, 115913-36-5; VI, 115913-37-6; VII, 115913-38-7; VIII, 115913-39-8; IX, 115913-40-1; X, 115913-41-2; XI, 106835-53-4; ClCH_2CN, 107-14-2; piperidine, 110-89-4; morpholine, 110-91-8; piperazine, 110-85-0.

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