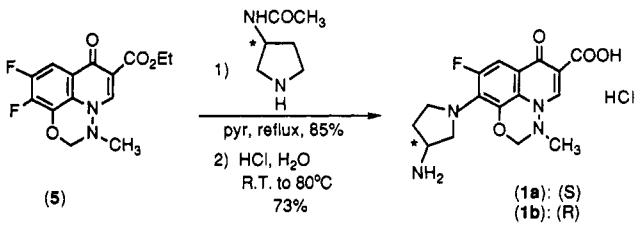
Scheme III



droxymethylated quinolone 4 at reflux under anhydrous conditions. In doing so, we were able to isolate the desired product **5** in good yield providing reaction times were kept short (Scheme I).

We attempted cyclization on a substrate in which the C-7 pyrrolidine was introduced prior to our hydroxymethylation–cyclization sequence (Scheme II). Pyrrolidine displacement of fluoride at C-7 occurred smoothly as reported,[15] and reaction with paraformaldehyde as previously described afforded hydroxymethylated quinolone **7** in excellent yield. However, all attempts to induce cyclization under the conditions successful for the trifluoro analogue **4** led only to deformylation (**6**) and tar formation. Apparently, the presence of the amino substituent at C-7 renders the aromatic system inert to fluoride-induced cyclization (as well as C-8 displacements in general[17]) via its electron-donating properties and/or its steric bulk.

With cyclized product **5** in hand, we were able to introduce either (*S*)- or (*R*)-3-aminopyrrolidine at C-7 to afford quinolone antibacterials **1a** and **1b**. Both pyrrolidines were prepared according to literature methods[22,23] and readily displaced fluoride at C-7 upon heating in pyridine.[15] Treatment of the corresponding adducts with aqueous acid accomplished removal of the amino *t*-Boc protecting group as well as ester cleavage as reported,[13-15] giving the final products **1a** and **1b** (Scheme III).

Experimental Section

6,7,8-Trifluoro-1,4-dihydro-1-[(hydroxymethyl)methylamino]-4-oxo-3-quinolinecarboxylic Acid Ethyl Ester (4). Ethyl 1-(Methylamino)-4-oxo-6,7,8-trifluoro-1,4-dihydro-3-quinoline carboxylate (**3**) (4.5 g, 15.0 mmol) and paraformaldehyde (20 g) were added to water (750 mL). The resulting heterogeneous mixture was heated at reflux for approximately 36 h and then cooled. The product was extracted into chloroform (3×) and the combined organic extracts were washed with water (2×). The organic solution was dried over magnesium sulfate and the solvent removed via rotary evaporation. The off-white solid obtained was further dried by vacuum pump to afford pure hydroxymethylated quinolone **4** (4.5 g, 90%): mp 138–139 °C; NMR (ppm, $CDCl_3$) 8.89 (s, 1 H, vinylic), 7.43 (ddd, J = 2,7,10 Hz, 1 H, aromatic), 5.90 (app t, 1 H, OH), 5.24 (AB dd, 1 H, NCH_2O), 4.60 (AB dd, 1 H, NCH_2O), 4.00–4.25 (m, 2 H, ester CH_2), 3.16 (s, 3 H, NMe), 1.32 (t, 3 H, CH_3); IR (cm^{-1}, $CHCl_3$) 3400 (b, OH), 2800–3050 (CH alkyl and aryl), 1730 (C=O ester), 1620 (C=O ketone); MS 330 (M^+), 312 ($M^+ - H_2O$), 300 ($M^+ - CH_2OH$).

3,7-Dihydro-9,10-difluoro-3-methyl-7-oxo-2*H*-pyrido[3,2,1-*ij*][1,3,4]benzoxadiazine-6-carboxylic Acid Ethyl Ester (5). The hydroxymethylated quinolone **4** (0.9 g, 2.72 mmol) was dissolved in dry tetrahydrofuran (205 mL) and heated to reflux as quickly as possible (<5 min). Tetrabutylammonium fluoride (6.0 mL of 1.0 M solution in THF, 6.0 mmol) was added as quickly as possible via syringe, and the mixture was heated at reflux for 22 min. After this time, the reaction mixture was poured into saturated sodium bicarbonate solution and the product was extracted into ethyl acetate (3×). The combined organic extracts were washed with brine solution and dried over sodium sulfate and the solvents removed by rotary evaporation. The remaining orange-brown oil was subjected to a silica gel plug (ethyl acetate) to obtain pure product as an off-white solid (434 mg). The plug was then "washed" with an ethyl acetate/methanol (3:1) solution to afford a tan residue from which more product was obtained via trituration with ethyl ether (85 mg). The total amount of pure product **5** isolated was 0.52 g, which represents a 61% yield: mp 274 °C dec; NMR (ppm, $CDCl_3$) 8.46 (s, 1 H, vinylic), 7.84 (dd, J = 7, 10 Hz, 1 H, aromatic), 5.12 (bs, 2 H, methylene), 4.40 (q, 2 H, CH_2), 3.05 (s, 3 H, NMe), 1.41 (t, 3 H, CH_3); ^{19}F NMR (ppm, $CHCl_3$) 151.0, 135.8; IR (cm^{-1}, $CHCl_3$) 2800–3050 (CH alkyl and aryl), 1720 (C=O ester), 1620 (C=O ketone); MS 310 (M^+), 265 ($M^+ - OEt$), 238 ($M^+ - CO_2Et$).

(*S*)-7-[3-(Acetylamino)-1-pyrrolidinyl]-6,8-difluoro-1,4-dihydro-1-[(hydroxymethyl)methylamino]-4-oxo-3-quinolinecarboxylic Acid Ethyl Ester (7). (*S*)-7-[3-(Acetylamino)-1-pyrrolidinyl]-6,8-difluoro-1,4-dihydro-1-(methylamino)-4-oxo-3-quinolinecarboxylic acid ethyl ester (**6**) (0.70 g, 1.71 mmol) and paraformaldehyde (2.3 g) were added to water (80 mL). The resulting heterogeneous mixture was heated at reflux for approximately 30 h and then cooled. The product was extracted into chloroform (3×), and the combined organic extracts were washed with water (2×). The organic solution was dried over magnesium sulfate and the solvent removed via rotary evaporation. The yellow solid obtained was further dried by vacuum pump to afford hydroxymethylated quinolone **7** (0.68 g, 90%): mp >150 °C dec; NMR (ppm, $CDCl_3$) 8.76 (s, 1 H, vinylic), 7.49 (d, 1 H, aromatic), 7.05 (d, 1 H, NH), 6.12 (bs, 1 H, OH), 5.20 (bs, 1 H, NCH_2O), 4.55 (bm, 2 H, NCH_2O and CHNHAc), 4.20–4.40 (m, 2 H, ester CH_2), 3.50–4.00 (4 H, pyrrolidinyl CH_2s), 3.10 (s, 3 H, NMe), 1.90–2.30 (m, 2 H, pyrrolidinyl CH_2), 2.07 (s, 3 H, CH_3), 1.38 (t, 3 H, CH_3); IR (cm^{-1}, $CHCl_3$) 3440 (NH), 3330 (b, OH), 2800–3050 (CH alkyl and aryl), 1720 (C=O ester), 1670 (C=O amide), 1610 (C=O ketone); MS 408 ($M^+ - CH_2O$), 379 ($M^+ - MeC(O)NH_2$), 320 ($M^+ - MeNCH_2OH$).

Acknowledgment. We wish to thank Dr. I. Kompis and his colleagues at Roche Basle along with Dr. D. D. Keith and Dr. M. Weigele at Roche Nutley for their help during the course of these studies. We are also thankful to Ms. BettyAnn Hedemus for the preparation of this manuscript.

Registry No. **1a**, 137435-04-2; **1a** free base, 137435-05-3; **1b**, 137435-06-4; **1b** free base, 137435-07-5; **3**, 100276-66-2; **4**, 137435-08-6; **5**, 137435-09-7; **6**, 137435-10-0; **7**, 137435-11-1; (*S*)-3-(acetylamino)pyrrolidine, 114636-31-6; (*R*)-3-(acetylamino)pyrrolidine, 131900-62-4.

Supplementary Material Available: NMR spectra of **3**, **4**, and **5** (5 pages). Ordering information is given on any current masthead page.

(22) Rosen, T.; Lico, I. M.; Chu, D. T. W. *J. Org. Chem.* **1988**, *53*, 1580.
(23) Rosen, T.; Chu, D. T. W.; Lico, I. M.; Prabharathi, B. F.; Shen, L.; Borodkin, S.; Pernet, A. G. *J. Org. Chem.* **1988**, *53*, 1580.

Synthesis of Hydrophenaleno[1,9-*bc*]thiophenes and [2]Metacyclo[2](2,4)thiophenophane

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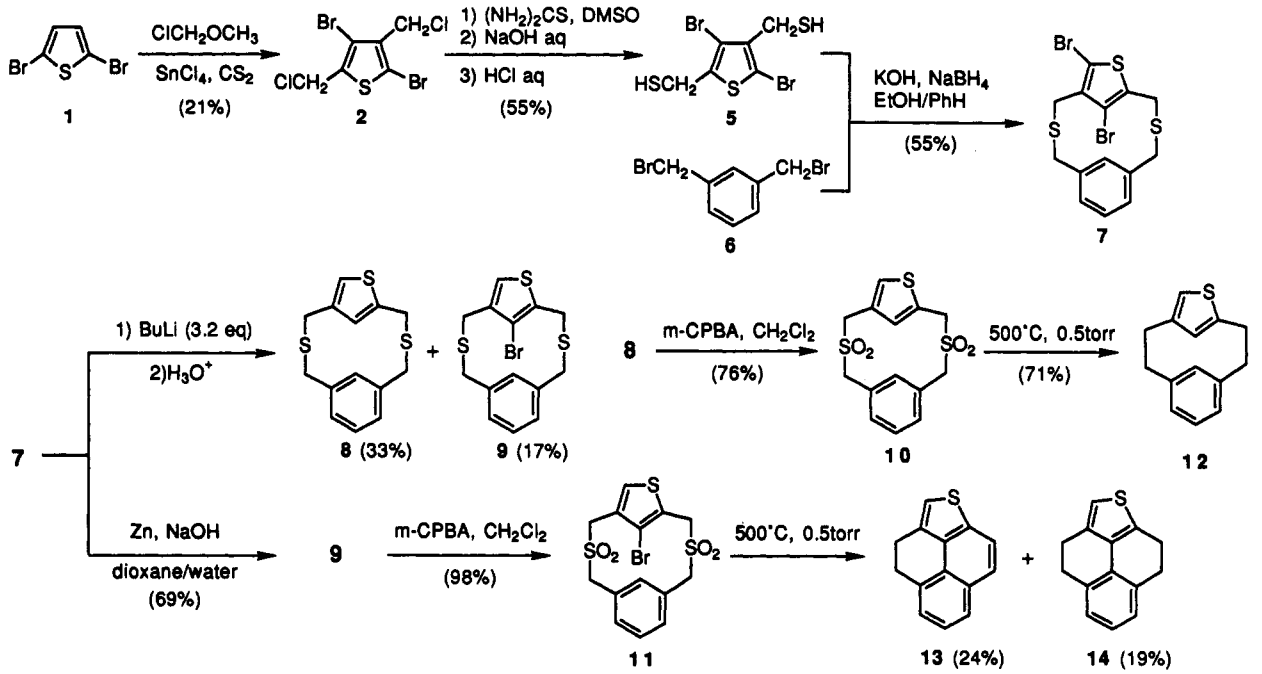
We have recently reported that metacyclo[2](2,3)-, -(2,4)-, -(2,5)-, and -(3,4)thiophenophane derivatives were prepared from the corresponding dithia[3]metacyclo[3]thiophenophanes.[1] However, except for the (2,5)phane system, unsubstituted parent compounds could not be obtained by this method. This result prompted us to try

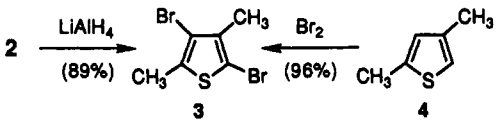
(1) Takeshita, M.; Tashiro, M. *J. Org. Chem.* **1991**, *56*, 2837.

0022-3263/92/1957-0746$03.00/0

Scheme I



Scheme II



synthesis of unsubstituted metacyclo(2,4)thiophenophanes from the corresponding dibromodithia[3]metacyclo[3]-(2,4)thiophenophane (5) using the bromine atom as a positional protective function.

3,5-Bis(chloromethyl)-2,4-dibromothiophene (2)[2] was obtained in 21% yield[3] by chloromethylation[4] of 2,5-dibromothiophene (1) with $ClCH_2OCH_3$ and $SnCl_4$ in CS_2 (Scheme I). Hydrodechlorination of 2 with $LiAlH_4$[5] afforded 2,4-dibromo-3,5-dimethylthiophene (3), which was also obtained from 2,4-dimethylthiophene[1] (4) by bromination with Br_2 (Scheme II).

The chloromethyl derivative 2 should be a good starting material for preparation of unsubstituted metacyclo-(2,4)thiophenophanes (8 and 12). Mercaptomethyl derivative 5, which was too labile to store for a long time, was obtained in a similar manner to that described in the literature.[1] Coupling of 5 and 6 under high dilution conditions[1] afforded dibromodithia[3.3]cyclophane 7. Removal of the bromine atoms of 7 was carried out in two ways. Treatment of 7 with BuLi and then water gave the expected product 8 in 33% yield plus monobromide 9. Compound 9 was also obtained in good yield by treatment of 7 with Zn in NaOH solution. The ^1H NMR spectra of the methylene group of 7 and 9 are observed as eight doublets at 27 °C, respectively, whereas the methylene chain of 8 is observed as four singlets. At 27 °C on the NMR time scale, the bulky Br atom at inner ortho position of 9 causes restricted motion which leads to anisotropy of the methylene protons while 8 is free to Ar–C–S "wobble"[1,6] so the methylene protons are averaged.

The desired [2]metacyclo[2](2,4)thiophenophane (12) was obtained via sulfone derivative 10 according to a reported method.[1,7] The obtained 12 should be the anti conformer because the ^1H NMR spectrum of the inner proton was observed at 4.08 ppm.

It was also found that pyrolysis of monobromo derivative 11, which was prepared from 9, afforded a mixture of phenaleno[1,9-*bc*]thiophene derivatives 13 and 14. Formation of methyl derivatives of phenaleno[1,9-*bc*]-thiophene was reported in the previous work.[1] The structure of 13 was assigned by analogy of the ^1H NMR spectrum to that of the corresponding methyl derivative.[1]

Experimental Section

All melting points are uncorrected. ^1H NMR spectra were recorded at 270 MHz.

2,4-Bis(chloromethyl)-3,5-dibromothiophene (2). To a stirred mixture of 35 g (0.25 mol) of 2,5-dibromothiophene (1), 64 g (0.80 mol) of chloromethyl methyl ether, and 190 mL of CS_2 at 0 °C was added dropwise a mixture of 77 g of $SnCl_4$ (0.30 mol) and 15 mL of CS_2 over a period of 2 h. The mixture was then stirred for 2.5 h at 0 °C at 1 h at room temperature and poured into ice/water. The organic phase was separated, washed with brine, and dried ($MgSO_4$). The solvent was evaporated, and the residue was extracted with 100 mL of hot hexane. Recrystallization of the extracts from hexane afforded 18 g (21%) of 2: colorless needles (hexane); mp 86.0–88.0 °C (lit.[4] mp 88.0–88.5 °C); IR (KBr) ν 1531, 1432, 1259, 1038, 902, 726, 639 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.56 (2 H, s), 4.70 (2 H, s); MS *m/e* 336, 338, 340 [M^+]. Anal. Calcd for $C_6H_4Br_2Cl_2S$: C, 21.27; H, 1.19. Found: C, 21.45; H, 1.34.

2,4-Dibromo-3,5-dimethylthiophene (3). To a solution of 1.7 g (5.0 mmol) of 2 in 30 mL of dry Et_2O was added gradually 570 mg (15 mmol) of $LiAlH_4$, and this mixture was refluxed under N_2 for 3 h. The reaction mixture was poured into ice/water, and the organic phase was separated, washed with brine, and dried ($MgSO_4$). Evaporation of the solvent afforded 1.2 g (89%) of 3: colorless oil; IR (NaCl) ν 2916, 1554, 1438, 1379, 1330, 1022, 952,

(2) The yield determined by GC was 40%.

(3) Synthesis of 2 by chloromethylation of 2,4-dibromothiophene: Hori, M.; Kataoka, T.; Shimizu, H.; Yoshimura, M. *Yakugaku Zasshi* **1974**, *94*, 1429; *Chem. Abstr.* **1975**, *82*, 170549h.

(4) The formation of 3,4-bis(chloromethyl)-2,5-dibromothiophene from 1 by the same method was reported: Sone, C. *Nippon Kagaku Kaishi* **1965**, *86*, 1185; *Chem. Abstr.* **1966**, *65*, 13636h.

(5) Johnson, J. E.; Blizzard, R. H.; Carhart, H. W. *J. Am. Chem. Soc.* **1948**, *70*, 3664.

(6) Mitchell, R. H. *Cyclophanes*; Keehn, P. M., Rosenfeld, S. M., Eds.; Academic Press: New York, 1983; Vol. 1, Chapter 4.

(7) For example: (a) Vögtle, F. *Chem. Ber.* **1967**, *102*, 3077. (b) Tashiro, M.; Yamato, T. *J. Org. Chem.* **1981**, *46*, 1543.

757 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.16 (3 H, s), 2.34 (3 H, s); HRMS m/e 267.8559 [M$^+$], calcd for $C_6H_6Br_2S$ 267.8558.

A mixture of 110 mg (1.0 mmol) of 2,4-dimethylthiophene (4) and 500 mg (3.1 mmol) of Br_2 was stirred for 3 min at rt. The organic product was extracted with CH_2Cl_2, and the extract was washed with brine and dried ($MgSO_4$). Evaporation of the solvent afforded 260 mg (96%) of 3.

2,4-Bis(mercaptomethyl)-3,5-dibromothiophene (5). A solution of 13.6 g (40 mmol) of 2 and 7.6 g (100 mmol) of thiourea in 100 mL of DMSO was stirred at room temperature for 13 h under N_2. The mixture was poured into 130 mL of 10% aq NaOH and stirred for 1 h in an ice/water bath. The mixture was acidified with 10% aq HCl, and the organic layer was extracted with CH_2Cl_2. The extract was washed with brine and dried ($MgSO_4$). The solvent was evaporated. Recrystallization of the residue from hexane afforded 7.3 g (55%) of 5: colorless prisms (hexane); mp 58.0–63.0 °C; IR (KBr) ν 2534, 1538, 1416, 1349, 1243, 1029, 954 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.95 (1 H, t, J = 8 Hz), 2.05 (1 H, t, J = 8 Hz), 2.64 (2 H, d, J = 8 Hz), 2.78 (2 H, d, J = 8 Hz); HRMS m/e 331.7994 [M$^+$], calcd for $C_6H_6Br_2S_3$ 331.7999.

14,17-Dibromo-2,11-dithia[3]metacyclo[3](2,4)thiophenophane (7). To a refluxing solution of 4.3 g (80 mmol) of KOH and 380 mg (10 mmol) of $NaBH_4$ in 3 L of EtOH was added dropwise a solution of 6.7 g (20 mmol) of 5 and 5.3 g (20 mmol) of 1,3-bis(bromomethyl)benzene (6) in 200 mL of EtOH:PhH = 1:1 over 23 h. The solvent was removed by distillation, and the residue was poured into ice/water. The organic layer was extracted with CH_2Cl_2, and the extract was washed with brine and dried ($MgSO_4$). The solvent was evaporated, and the residue was subjected to column chromatography (silica gel, eluent: hexane:CH_2Cl_2 = 2:1). Recrystallization of the eluate afforded 4.8 g (55%) of 7: colorless prisms (EtOH/PhH); mp 137.0–138.0 °C; IR (KBr) ν 2902, 1542, 1443, 1409, 1342, 1212, 1025, 931, 909, 886, 771, 709 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.62 (1 H, d, J = 14 Hz), 3.65 (1 H, d, J = 15 Hz), 3.74 (1 H, d, J = 15 Hz), 3.78 (1 H, d, J = 17 Hz), 3.89 (1 H, d, J = 15 Hz), 3.92 (1 H, d, J = 14 Hz), 3.93 (1 H, d, J = 17 Hz), 4.58 (1 H, d, J = 15 Hz), 7.02–7.17 (4 H, m); MS m/e 434, 436, 438 [M$^+$]. Anal. Calcd for $C_{14}H_{12}Br_2S_3$: C, 38.54; H, 2.77. Found: C, 38.93; H, 2.89.

Hydrodebromination of 7. 1. Via Lithiation. A solution of 870 mg (2.0 mmol) of 7 in 20 mL of dry THF at −60 °C was added to 4.0 mL (6.4 mmol) of 1.6 M BuLi in hexane, and the mixture was stirred for 40 min at this temperature. The mixture was treated with 5 mL of 10% aq HCl, stirred for 1 h at room temperature, and extracted with Et_2O. The extract was washed with brine and dried ($MgSO_4$). The solvent was evaporated, and the residue was subjected to column chromatography (silica gel eluent: hexane:CH_2Cl_2 = 3:1). Recrystallization of the first eluate afforded 120 mg (17%) of 9 and that of the second eluate afforded 180 mg (33%) of 8.

2,11-Dithia[3]metacyclo[3](2,4)thiophenophane (8): colorless prisms (hexane) mp 133.0–135.0 °C; IR (KBr) ν 2900, 1489, 1442, 1408, 1249, 1116, 1082, 803, 758, 722, 707 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.70 (2 H, s), 3.80 (2 H, s), 3.81 (2 H, s), 4.01 (2 H, s), 6.56 (1 H, m), 6.74 (1 H, s), 6.79 (1 H, s), 6.87 (1 H, dt, J = 6, 2 Hz), 7.04–7.07 (2 H, m); MS m/e 278 [M$^+$]. Anal. Calcd for $C_{14}H_{14}S_3$: C, 60.39; H, 5.07. Found: C, 60.72; H, 5.34.

17-Bromo-2,11-dithia[3]metacyclo[3]-(2,4)-thiophenophane (9): colorless prisms (hexane); mp 141.0–143.0 °C; IR (KBr) ν 2900, 1528, 1488, 1442, 1410, 1364, 1219, 1084, 992, 892, 769, 720; ^{1}H NMR ($CDCl_3$) δ 3.71 (1 H, d, J = 15 Hz), 3.74 (1 H, d, J = 15 Hz), 3.75 (1 H, d, J = 15 Hz), 3.84 (1 H, d, J = 15 Hz), 3.85 (1 H, d, J = 15 Hz), 3.86 (1 H, d, J = 15 Hz), 3.90 (1 H, d, J = 15 Hz), 4.57 (1 H, dd, J = 15, 2 Hz), 6.68 (1 H, s), 6.91–6.97 (2 H, m), 7.03–7.13 (2 H, m); MS m/e 356, 358 [M$^+$]. Anal. Calcd for $C_{14}H_{13}BrS_3$: C, 47.05; H, 3.67. Found: C, 47.37; H, 3.97.

2. Treatment with Zn. A mixture of 2.0 g (4.5 mmol) of 7, 860 mg (13.5 mmol) of Zn, and 1.08 g (18 mmol) of NaOH in 9 mL of water and 45 mL of dioxane was refluxed for 24 h. The mixture was acidified with 10% aq HCl and filtered. The filtrate was extracted with CH_2Cl_2, and the extract was washed with brine and dried ($MgSO_4$). The solvent was evaporated. Recrystallization of the residue afforded 1.14 g (69%) of 9.

2,11-Dithia[3]metacyclo[3](2,4)thiophenophane *S,S,S',S'*-*S'*-Tetraoxide (10). To a solution of 140 mg (0.50 mmol) of 8 in 15 mL of CH_2Cl_2 was added portionwise 540 mg (2.5 mmol) of 80% *m*-CPBA, and the mixture was stirred at room temperature for 13 h. To the mixture was added 30 mL of MeOH, and the white precipitate was filtered and washed with MeOH and hot $CHCl_3$ to afford 130 mg (76%) of 10: colorless prisms; mp 320.0 °C dec; IR (KBr) ν 2914, 1406, 1310, 1269, 1168, 1110, 525, 463 cm^{-1}; a ^{1}H NMR spectrum was not recorded because 10 is insoluble in any solvent; MS m/e 342 [M$^+$]. Anal. Calcd for $C_{14}H_{14}O_4S_3$: C, 49.10; H, 4.12. Found: C, 48.75; H, 4.26.

17-Bromo-2,11-dithia[3]metacyclo[3](2,4)thiophenophane *S,S,S',S'*-tetraoxide (11) was obtained in a similar manner to that described above for 10. 11: colorless prisms mp 295.0 °C dec; IR (KBr) ν 2974, 2914, 1404, 1317, 1274, 1168, 1115, 861, 460 cm^{-1}; a ^{1}H NMR spectrum was not recorded because 11 is insoluble in any solvent; MS m/e 420, 422 [M$^+$]. Anal. Calcd for $C_{14}H_{13}BrO_4S_3$: C, 39.91; H, 3.11. Found: C, 40.37; H, 3.25.

Pyrolysis of 10. Pyrolysis of 120 mg (0.35 mmol) of 10 was performed in similar manner to that described in the literature.[7] The products were extracted with CH_2Cl_2, and the insoluble ash was filtered off. The solvent was evaporated, and recyrstallization of the residue afforded 53 mg (71%) of **[2]metacyclo[2](2,4)-thiophenophane (12)**: colorless prisms (60% MeOH); mp 92.0–93.0 °C; IR (KBr) ν 2938, 2846, 1439, 1238, 1169, 791, 716 670 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.23–2.49 (4 H, m), 2.95–3.15 (4 H, m), 4.08 (1 H, d, J = 1 Hz), 4.63 (1 H, t, J = 2 Hz), 6.99 (1 H, s), 7.02 (2 H, t, J = 7 Hz), 7.20 (1 H, t, J = 7 Hz); MS m/e 214 [M$^+$]. Anal. Calcd for $C_{14}H_{14}S$: C, 78.46; H, 6.58. Found: C, 78.22; H, 6.52.

Pyrolysis of 420 mg (1.0 mmol) of 11 was carried out in a similar manner to that described above, and the extract was subjected to column chromatography (*silica gel, eluent: hexane*). Recrystallization of first eluate afforded 40 mg (19%) of 13, and that of second eluate afforded 50 mg (24%) of 14.

8,9-Dihydrophenaleno[1,9-*bc*]thiophene (13): colorless plates (60% MeOH); mp 120.0–123.0 °C; IR (KBr) ν 2930, 1396, 819, 762, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.21–3.27 (2 H, m), 3.31–3.38 (2 H, m), 7.15 (1 H, s), 7.38–7.49 (2 H, m), 7.72 (1 H, d, J = 9 Hz), 7.76–7.79 (1 H, m), 7.85 (1 H, d, J = 9 Hz); MS m/e 210 [M$^+$]. Anal. Calcd for $C_{14}H_{10}S$: C, 79.96; H, 4.79. Found: C, 80.21; H, 5.02.

3,4,8,9-Tetrahydrophenaleno[1,9-*bc*]thiophene (14): colorless plates (60% MeOH); mp 134.0–140.0 °C IR (KBr) ν 2930, 2890, 1601, 1560, 1494, 1428, 1110, 794, 769, 735, 686 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.84–2.95 (4 H, m), 2.94–3.08 (4 H, m), 6.74 (1 H, s), 7.06–7.07 (3 H, m); MS m/e 212 [M$^+$]. Anal. Calcd for $C_{14}H_{12}S$: C, 79.20; H, 5.70. Found: C, 78.98; H, 5.74.

Registry No. 1, 3141-27-3; 2, 7311-54-8; 3, 63862-00-0; 4, 638-00-6; 5, 137434-94-7; 6, 626-15-3; 7, 137434-95-8; 8, 137434-96-9; 9, 137434-97-0; 10, 137434-98-1; 11, 137434-99-2; 12, 137435-00-8; 13, 137435-01-9; 14, 137435-02-0; chloromethyl methyl ether, 107-30-2; thiourea, 62-56-6.

Cyanoacylation of 1-Substituted Isoquinolines and 3,4-Dihydroisoquinolines

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Reissert compounds such as 2-acyl-1-cyano-1,2-dihydroisoquinolines, their reactions, and, to a lesser extent, dihydro-Reissert compounds such as 2-acyl-1-cyano-1,2,3,4-tetrahydroisoquinolines have been well documented.[1] Reissert compounds are typically formed by treating an isoquinoline or 3,4-dihydroisoquinoline with an acyl halide in the presence of potassium cyanide in biphasic aqueous dichloromethane.[2] It was shown that

(1) Cooney, J. V. *J. Heterocycl. Chem.* **1983**, *20*, 823–837 and references cited therein.

0022-3263/92/1957-0748$03.00/0