# Synthesis and functionalization of thiophene congeners of Tröger's base

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Thiophene congeners of Tröger's base were prepared by the reactions of 3-aminothiophenes and formaldehyde. Treatment of the thiophene congeners with BuLi or LDA resulted in the regioselective formation of the dianion at the 2- and 7-positions, which reacted with a variety of electrophiles such as trimethylsilyl chloride, iodine, NBS, DMF, benzophenone, and benzaldehyde. This reaction opens up a facile and versatile entry for a Tröger's base skeleton with a variety of functional groups.

## Introduction

Tröger's base **1** with a bridged methanodiazocine skeleton has been recognized as the first chiral tertiary amine which can be resolved.[1,2] Recently, Tröger's base and its analogues have received much attention in the study of CH-π interactions,[3–5] host molecules as molecular tweezers,[6–13] and cyclophanes.[14–19] Tröger's base **1** is obtained by the reaction of *p*-toluidine and formaldehyde under acidic conditions. However, the syntheses of Tröger's base analogues were restricted to the use of aniline derivatives with alkyl or electron-donating substituents at the *para*-position, and the syntheses with aniline derivatives bearing electron-withdrawing groups such as halogen and formyl groups was reported to be unsuccessful.[1,20–24] On the other hand, the treatment of **1** with butyllithium (BuLi)–boron trifluoride–diethyl ether was found to undergo abstraction of the methylene proton adjacent to the aromatic ring;[25,26] direct functionalization on the aromatic rings seems to be difficult. These results motivated us to prepare a thiophene congener of Tröger's base, because the functionalization of a thiophene ring has been well investigated both by electrophilic substitution reactions and the nucleophilic reaction of thienyl metals.[27–30] Therefore, the synthesis of a thiophene congener of Tröger's base is expected to open up a new pathway toward the Tröger's base analogues with a variety of functional groups.

Although the heterocyclic analogues of **1** with phenanthroline,[31,32] porphyrin,[33,34] acridine,[35–38] pyrazole,[39] and benzothiophene *S,S*-dioxide[40] rings have been previously reported, no attempt to synthesize a thiophene congener of **1** has been described so far.

## Results and discussion

A mixture of 3-aminothiophene[41] (**2**), formaldehyde and hydrochloric acid in methanol was stirred at room temperature for 13 h to provide 4,5,9,10-tetrahydro-4,9-methanodithieno-[3,2-*b*:3′,2′-*f*][1,5]diazocine (**4**) in 24% yield. Although the yield of **4** is moderate, we could not observe the formation of other products or the recovery of **2**. The $^{13}$C-NMR spectrum of **4** exhibits six peaks in agreement with the structure of **4** with $C_2$ symmetry. The $^1$H-NMR spectrum of **4** shows the protons of the thiophene ring at $\delta_H$ 6.81 and 7.09 as doublet with a coupling constant of 5 Hz. This indicates that the fusion of the thiophene ring takes place between the 2- and 3-positions of the thiophene ring. Our attempts to synthesize **4** by the use of hexamethylenetetraamine and trifluoroacetic acid[22] or dimethoxymethane and methanesulfonic acid[23] resulted in the formation of a complex mixture. The reaction of 3-amino-4-methylthiophene[42] (**3**) with formaldehyde similarly provided **5** in 15% yield (Scheme 1).

In the case of the reaction with **2**, we also isolated a trace amount (<1%) of dithieno[3,2-*b*:2′3′-*e*]pyridine[43] (**6**). When a similar reaction was carried out under reflux, the dithienopyridine **6** was obtained in 11% yield. On the other hand, when the thiophene **4** was treated with hydrochloric acid under the same conditions as the synthesis of **4**, we obtained no evidence for the formation of **6**. When a solution of the thiophene **4** in methanol was heated under reflux in the presence of hydrochloric acid compound **6** was formed in 43% yield. The latter reaction would be a practical method for the preparation of **6**.[43] Although we could not clarify the mechanism for the formation of **6**, the intervention of a quinone-imine-methide intermediate was suggested for a similar transformation of an acridine-fused Tröger's base to a fused pyridine.[44]

Attempted electrophilic reactions of the thiophene congener **4** with bromine or *N*-bromosuccinimide (NBS), and the Friedel–Crafts acylation reaction resulted in the formation of a complex mixture. Therefore we turned to the investigation of the formation of the dianion of **4** with BuLi which is widely recognized in the literature.[28–30]

The thiophene **4** was treated with three molar equivalents of BuLi followed by quenching with $D_2O$ to result in the regioselective formation of 2,7-dideuterio derivative **7** in 53% yield. Although the yield of **7** is moderate, we could not observe the formation of a mono-deuterio product or other products. Furthermore, the use of two molar equivalents of BuLi resulted in the partial recovery of **4**, and the use of four molar equivalents of BuLi did not increase the yield of **7**. Under similar conditions, treatment with trimethylsilyl chloride, iodine, or NBS as an electrophilic reagent provided the 2,7-disubstituted derivatives **8**, **9**, and **10**, respectively. The formylation reaction of **4** with DMF seemed to be more effective and the 2,7-dicarbaldehyde **11** was obtained in 59% yield. Similarly, the methyl-substituted derivative **5** also afforded **12** in 53% yield: substitution of the methyl groups did not affect the formation of the dianion. On treatment with benzophenone, the 2,7-bis(hydroxydiphenylmethyl) derivative **13** was produced in 51% yield. When benzaldehyde was employed as an electrophilic reagent, two diastereoisomers were formed: one is the 2,7-bis(hydroxyphenyl-

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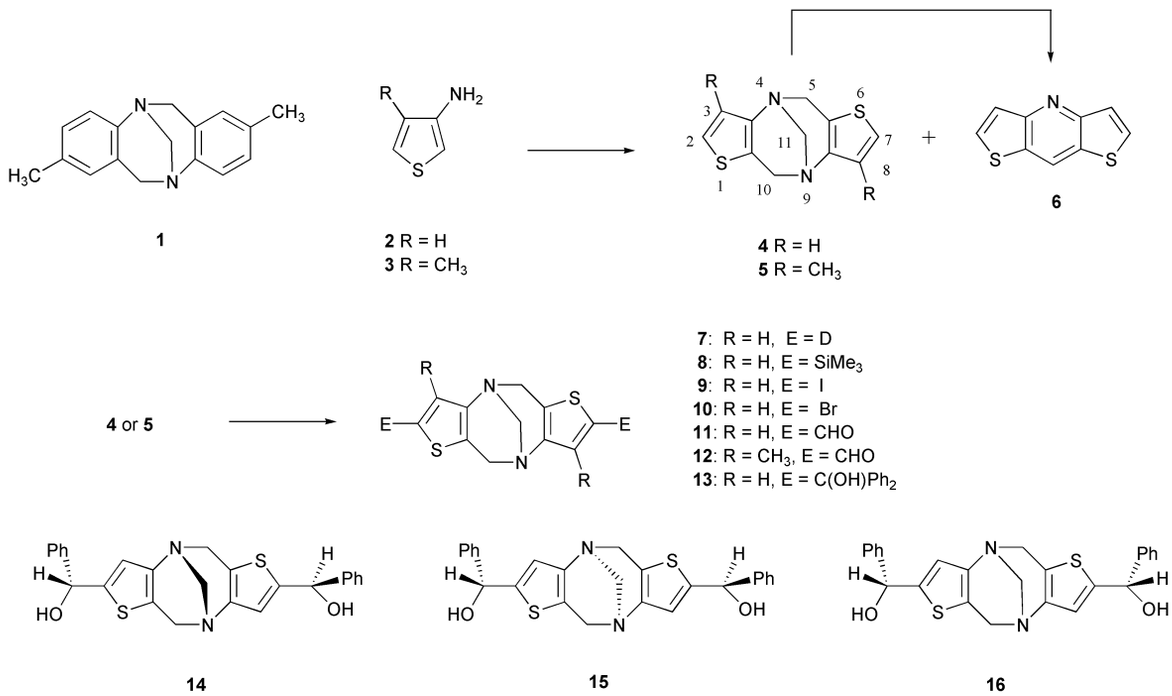


**Scheme 1**

methyl) derivative **14** or **15** with $C_2$ symmetry and the other is the derivative **16** without a symmetrical axis.

Lithium diisopropylamide (LDA) was also found to effect the formation of the dianion. Treatment of **4** with LDA followed by addition of iodine gave **9** in 61% yield. The yield is better than that with BuLi, probably due to inhibition of the halogen–metal exchange reaction which might take place with BuLi. Unfortunately, the reaction of **4** with LDA and the following treatment with NBS or DMF resulted in decrease of the yields when compared to those with BuLi. Furthermore, the use of magnesium chloride diisopropylamide[30] ($i$Pr$_2$NMgCl) as a base did not work for the present reaction and the starting substrate was recovered.

In conclusion, we have demonstrated that the thiophene congeners of Tröger's base were prepared by the reactions of 3-aminothiophenes and formaldehyde. Treatment of the thiophene congeners with BuLi or LDA underwent the regioselective formation of the dianion at the 2- and 7-positions, which opened up a facile and versatile entry for the preparation of the functionalized Tröger's base skeleton with a variety of substituents. In particular, the dicarbaldehydes **11** and **12** as well as the hydroxymethyl derivatives **13**–**16** would be useful for the construction of new molecular tweezers. We are currently extending our investigations to potential molecular recognition and supramolecular chemistry, and these results will be reported in due course.

## Experimental

### General

All the melting points were determined with a Yanagimoto hot-stage apparatus. IR spectra were obtained with a JEOL Diamond-20 spectrometer. NMR spectra were recorded with either JEOL JNM-LA300 ($^1$H: 300 MHz, $^{13}$C: 75 MHz) or JEOL JNM-LA400 ($^1$H: 400 MHz, $^{13}$C: 100 MHz) spectrometers using TMS as internal standard. *J*-Values are given in Hz. Assignments of the $^1$H and $^{13}$C signals are based on DEPT, H–H COSY, and C–H COSY measurements. The symbols "H$_x$" and "H$_n$" in the assignment represent *exo* and *endo* protons, respectively. Mass spectra were measured with a Shimadzu GCMS-QP1000EX spectrometer operating in the electron impact mode (70 eV). Elemental analyses were performed with a Perkin–Elmer Model 240 apparatus. MPLC separations were conducted by a YAMAZEN YFLC-600–10V system with a YAMAZEN Ultra Pack® Column (Si-40B, Silica Gel). All the reactions were carried out under nitrogen atmosphere. Solvents were dried and purified by standard methods. Yields are based on isolated products.

### 4,5,9,10-Tetrahydro-4,9-methanodithieno[3,2-*b*:3′,2′-*f*][1,5]-diazocine 4

A mixture of 3-aminothiophene oxalate[41] (**2**-oxalate) (8.120 g 43 mmol), formaldehyde (35%, 22.12 g, 258 mmol), aqueous HCl (35%, 22.40 g, 215 mmol) in methanol (40 cm$^3$) was stirred at room temperature for 13 h. The reaction mixture was poured into an aqueous ammonia solution (4%, 350 cm$^3$) and extracted with dichloromethane. The combined organic phases were washed with aqueous sodium hydrogencarbonate and brine prior to drying with $Na_2SO_4$. After removal of the solvent, the residue was separated by column chromatography (silica gel, hexane–ethyl acetate 2 : 1) to give **4** (1.217 g, 24%) as colorless needles (from methanol); mp 170–171 °C (Found: C, 56.5; H, 4.0; N, 12.1. $C_{11}H_{10}N_2S_2$ requires C, 56.4; H, 4.3; N, 11.95%); $\nu_{max}$(KBr)/cm$^{-1}$ 3099, 3085, 2942, 2937, 1540, 1390; $\delta_H$($CDCl_3$, 400 MHz) 4.12 (2H, d, *J* 16, 5-H$_n$ and 10-H$_n$), 4.22 (2H, s, 11-H), 4.55 (2H, d, *J* 16, 5-H$_x$ and 10-H$_x$), 6.81 (2H, d, *J* 5, 3-H and 8-H), 7.09 (2H, d, *J* 5, 2-H and 7-H); $\delta_H$($CDCl_3$, 100 MHz) 53.7 (C-5 and C-10), 68.0 (C-11), 122.7 (C-2 and C-7), 123.0 (C-5a and C-10a), 123.4 (C-3 and C-8), 145.5 (C-3a and C-8a); *m*/*z* 234 (M$^+$, 100%), 206 (14), 124 (38), 97 (32), 80 (34), 45 (CHS, 60).

In this reaction, dithieno[3,2-*b*:2′3′-*e*]pyridine (**6**) was also isolated with a trace amount (10–20 mg) depending on each run.

**6**: Colorless needles (from methanol); mp 122–124 °C (decomp.) (lit.,[43] mp 106 °C) (Found: C, 56.7; H, 2.6; N, 7.6. $C_9H_5NS_2$ requires C, 56.5; H, 2.6; N, 7.3%); $\nu_{max}$(KBr)/cm$^{-1}$ 3043, 1537, 1371; $\delta_H$($CDCl_3$, 400 MHz) 7.61 (2H, dd, *J* 6 and 0.8, 3-H and 5-H), 7.81 (2H, d, *J* 6, 2-H and 6-H), 8.68 (1H, d, *J* 0.8, 8-H); $\delta_C$($CDCl_3$, 100 MHz) 124.4 (C-8), 124.7 (C-3 and C-5), 129.6 (C-7a and C-8a), 131.3 (C-2 and C-6), 155.1 (C-3a and C-4a); COLOC (correlation spectroscopy *via* long-range coupling system): cross peaks were observed between 8-H and C-7a and between 3-H and C-3a, not observed between 8-H

**Table 1** Functionalization of the dithienodiazocines **4** and **5**

| Substrate | R | Base | Electrophile | E | Products (Yield, %) |
|---|---|---|---|---|---|
| **4** | H | BuLi | $D_2O$ | D | **7** (53) |
| **4** | H | BuLi | $Me_3SiCl$ | $Me_3Si$ | **8** (31) |
| **4** | H | BuLi | $I_2$ | I | **9** (26) |
| **4** | H | BuLi | NBS | Br | **10** (24) |
| **4** | H | BuLi | DMF | CHO | **11** (59) |
| **5** | Me | BuLi | DMF | CHO | **12** (53) |
| **4** | H | BuLi | $Ph_2CO$ | C (OH) $Ph_2$ | **13** (51) |
| **4** | H | BuLi | PhCHO | CH(OH)Ph | **14** or **15** (15), **16** (23) |
| **4** | H | LDA | $I_2$ | I | **9** (61) |
| **4** | H | LDA | NBS | Br | **10** (15) |
| **4** | H | LDA | DMF | CHO | **11** (25) |

and C-3a and between 3-H and C-8a; *m*/*z* 191 ($M^+$, 100%), 45 (CHS, 15).

### 4,5,9,10-Tetrahydro-3,8-dimethyl-4,9-methanodithieno[3,2-*b*:3′,2′-*f*][1,5]diazocine 5

By a similar procedure as described for **4**, the reaction of 3-amino-4-methylthiophene oxalate[42] (**3**-oxalate) (1.016 g, 5 mmol), formaldehyde (35%, 2.572 g, 30 mmol), aqueous HCl (35%, 2.605 g, 25 mmol) in methanol (8 $cm^3$) provided **5** (101 mg, 15%) as colorless needles (from methanol); mp 168–169 °C (Found: C, 59.4; H, 5.1; N, 10.7. $C_{13}H_{14}N_2S_2$ requires C, 59.5; H, 5.4; N, 10.7%); $\nu_{max}$(KBr)/$cm^{-1}$ 3084, 2964, 2898, 2844, 1560, 1444, 1400, 1375, 1315; $\delta_H$($CDCl_3$, 400 MHz) 2.21 (6H, s, $CH_3$), 4.01 (2H, d, *J* 16, 5-$H_n$ and 10-$H_n$), 4.20 (2H, s, 11-H), 4.51 (2H, d, *J* 16, 5-$H_x$ and 10-$H_x$), 6.73 (2H, s, 2-H and 7-H); $\delta_C$($CDCl_3$, 100 MHz) 12.9 ($CH_3$), 51.6 (C-5 and C-10), 68.5 (C-11), 117.7 (C-2 and C-7), 123.7 (C-5a and C-10a), 132.5 (C-3 and C-8), 144.0 (C-3a and C-8a); *m*/*z* 262 ($M^+$, 100%), 234 (37), 138 (29), 126 (23), 105 (11), 67 (20), 45 (CHS, 35).

### Formation of the dithienopyridine 6 from the dithienodiazocine 4

A solution of the dithienodiazocine **4** (117 mg, 0.5 mmol) and HCl (35%, 0.5 $cm^3$) in methanol (1 $cm^3$) was refluxed for 19 h under a nitrogen atmosphere. Aqueous ammonia solution (4%, 15 $cm^3$) was added to the mixture, and the product was extracted by dichloromethane. The organic phase was washed with brine, and dried over $Na_2SO_4$. After removal of the solvent, the resulting solid was collected by suction to give **6** (41 mg, 43%): mp and mixed mp 122–124 °C.

### Formation of the dithienopyridine 6 from 3-aminothiophene (2)

A mixture of 3-aminothiophene oxalate (**2**-oxalate) (946 mg, 5 mmol), formaldehyde (35%, 214 mg, 2.5 mmol), aqueous HCl (35%, 2.61 g, 25 mmol) in methanol (5 $cm^3$) was heated under reflux for 24 h. The reaction mixture was poured into an aqueous ammonia solution and extracted with dichloromethane. The combined organic phases were washed with aqueous sodium hydrogencarbonate and brine prior to drying with $Na_2SO_4$. After removal of the solvent, the residue was separated by column chromatography (silica gel, dichloromethane) to give **6** (53 mg, 11%): mp and mixed mp 121–123 °C.

When a large excess of formaldehyde (35%, 2.574 g, 30 mmol) was used for the present reaction, **6** was obtained in 4% yield (17 mg).

### General procedure for the formation of the dianion of the dithienodiazocines 4 and 5 with BuLi or LDA and the functionalization with electrophiles

To a cooled solution (0 °C) of the dithienodiazocine **4** or **5** (0.5 mmol) in THF (5 $cm^3$), was added a solution of BuLi in hexane (1.5 M, 1.0 $cm^3$, 1.5 mmol) over 5 min under a nitrogen atmosphere. When LDA was employed as a base, a solution of LDA in THF was prepared by the reaction of diisopropylamine (152 mg, 1.5 mmol) and BuLi (1.5 M, 1 $cm^3$, 1.5 mmol) in THF (3 $cm^3$). The mixture was stirred at room temperature for 30 min, and cooled to −78 °C. To the cooled solution was added a solution of an electrophilic reagent (1.5 mmol) in THF (2 $cm^3$). The solution was warmed up to room temperature and stirred for 30 min. Water or aqueous sodium thiosulfate solution (in the cases with $I_2$ and NBS) was added to the mixture, and the products were extracted with dichloromethane (×3). The combined organic phases were washed with brine prior to drying over $Na_2SO_4$. After removal of the solvent, the residue was separated by MPLC (hexane–ethyl acetate 2 : 1 or 1 : 3) to give the products as listed in Table 1.

**2,7-Dideuterio-4,5,9,10-tetrahydro-4,9-methanodithieno-[3,2-*b*:3′,2′-*f*][1,5]diazocine 7.** A white solid; mp 169–171 °C; $\delta_H$($CDCl_3$, 400 MHz) 4.12 (2H, d, *J* 16, 5-$H_n$ and 10-$H_n$), 4.22 (2H, s, 11-H), 4.56 (2H, d, *J* 16, 5-$H_x$ and 10-$H_x$), 6.81 (2H, s, 3-H and 8-H); *m*/*z* 236 ($M^+$, 100%), 208 (14), 125 (37), 98 (32), 81 (35), 46 (CDS, 56).

**4,5,9,10-Tetrahydro-2,7-bis(trimethylsilyl)-4,9-methano-dithieno[3,2-*b*:3′,2′-*f*][1,5]diazocine 8.** Colorless rods (from hexane); mp 154–155 °C (Found: C, 53.7; H, 7.0; N, 7.4. $C_{17}H_{26}N_2S_2Si_2$ requires C, 53.9; H, 6.9; N, 7.4%); $\nu_{max}$(KBr)/$cm^{-1}$ 2949, 2924, 2908, 1535, 1444, 1435, 1371, 1350; $\delta_H$($CDCl_3$, 400 MHz) 0.27 (18H, s, $SiMe_3$), 4.15 (2H, s, 11-H), 4.16 (2H, d, *J* 16, 5-$H_n$ and 10-$H_n$), 4.58 (2H, d, *J* 16, 5-$H_x$ and 10-$H_x$), 6.95 (2H, s, 3-H and 8-H); $\delta_C$($CDCl_3$, 100 MHz) 0.05 ($SiMe_3$), 54.1 (C-5 and C-10), 67.9 (C-11), 128.5 (C-5a and C-10a), 130.4 (C-3 and C-8), 137.2 (C-2 and C-7), 147.1 (C-3a and C-8a); *m*/*z* 378 ($M^+$, 100%), 377 (M − H, 93), 363 (M − $CH_3$, 27), 350 (34), 273 (11), 196 (13), 174 (23), 73 ($SiMe_3$, 84), 45 (CHS, 14).

**4,5,9,10-Tetrahydro-2,7-diiodo-4,9-methanodithieno[3,2-*b*:3′,2′-*f*][1,5]diazocine 9.** A light tan solid (from chloroform–methanol 1 : 3); mp 195–203 °C (decomp.) (Found: C, 27.1; H, 1.75; N, 5.5. $C_{11}H_8I_2N_2S_2$ requires C, 27.2; H, 1.7; N, 5.8%); $\nu_{max}$(KBr)/$cm^{-1}$ 3085, 2941, 2902, 2844, 1535, 1429, 1377, 1350; $\delta_H$($CDCl_3$, 400 MHz) 4.00 (2H, d, *J* 16, 5-$H_n$ and 10-$H_n$), 4.12 (1H, s, 11-H), 4.42 (2H, d, *J* 16, 5-$H_x$ and 10-$H_x$), 6.94 (2H, s, 3-H and 8-H); $\delta_C$($CDCl_3$, 75 MHz) 53.4 (C-5 and C-10), 67.8 (C-11), 70.9 (C-2 and C-7), 128.9 (C-5a and C-10a), 132.8 (C-3 and C-8), 146.5 (C-3a and C-8a); *m*/*z* 486 ($M^+$, 100%), 359 (17, M − I), 250 (31), 96 (33).

**2,7-Dibromo-4,5,9,10-tetrahydro-4,9-methanodithieno[3,2-*b*:3′,2′-*f*][1,5]diazocine 10.** A light tan solid (from methanol); mp 179–180 °C (Found: C, 33.4; H, 2.0; N, 7.0. $C_{11}H_8Br_2N_2S_2$ requires C, 33.7; H, 2.1; N, 7.1%); $\nu_{max}$(KBr)/$cm^{-1}$ 3049, 2952, 2918, 2856, 1542, 1454, 1435, 1385, 1352; $\delta_H$($CDCl_3$, 400 MHz) 3.97 (2H, d, *J* 16, 5-$H_n$ and 10-$H_n$), 4.15 (2H, s, 11-H), 4.38 (2H, d, *J* 16, 5-$H_x$ and 10-$H_x$), 6.76 (2H, s, 3-H and 8-H); $\delta_C$($CDCl_3$, 100 MHz) 53.1 (C-5 and C-10), 67.7 (C-11), 110.5 (C-2 and C-7), 124.7 (C-5a and C-10a), 126.0 (C-3 and C-8), 145.1 (C-3a and C-8a); *m*/*z* 394/392/390 ($M^+$, 56/100/49%), 364 (13),

313/311 (M − Br, 33/34), 280 (11), 278 (10), 232 (11), 204 (42), 202 (42), 123 (73), 96 (86), 69 (30), 45 (CHS, 32).

**4,5,9,10-Tetrahydro-4,9-methanodithieno[3,2-*b*:3′,2′-*f*][1,5]-diazocine-2,7-dicarbaldehyde 11.** Light yellow plates (from chloroform–methanol 1 : 3); mp 255–256 °C (Found: C, 54.0; H, 3.4; N, 9.9. $C_{13}H_{10}N_2O_2S_2$ requires C, 53.8; H, 3.5; N, 9.65%); $\nu_{max}$(KBr)/cm$^{-1}$ 3084, 3049, 2964, 2941, 2924, 2821, 2798, 1664, 1537, 1452, 1427, 1410; $\delta_H$($CDCl_3$, 400 MHz) 4.20 (2H, d, *J* 17, 5-$H_n$ and 10-$H_n$), 4.24 (2H, s, 11-H), 4.63 (2H, d, *J* 17, 5-$H_x$ and 10-$H_x$), 7.50 (2H, s, 3-H and 8-H), 9.81 (2H, s, CHO); $\delta_C$($CDCl_3$, 100 MHz) 54.4 (C-5 and C-10), 67.6 (C-11), 131.9 (C-3 and C-8), 134.3 (C-5a and C-10a), 140.7 (C-2 and C-7), 146.5 (C-3a and C-8a), 182.3 (CHO); *m*/*z* 290 ($M^+$, 100%), 261 (M − CHO, 15), 140 (14), 97 (19), 95 (14), 80 (19), 53 (44), 45 (CHS, 38).

**4,5,9,10-Tetrahydro-3,8-dimethyl-4,9-methanodithieno[3,2-*b*:3′,2′-*f*][1,5]diazocine-2,7-dicarbaldehyde 12.** Yellow rods (from methanol); mp 256–258 °C (Found: C, 56.6; H, 4.4; N, 8.5. $C_{15}H_{14}N_2O_2S_2$ requires C, 56.6; H, 4.4; N, 8.8%); $\nu_{max}$(KBr)/cm$^{-1}$ 2954, 2912, 2821, 1657, 1649, 1468, 1427, 1381, 1369; $\delta_H$($CDCl_3$, 300 MHz) 2.54 (6H, s, $CH_3$), 4.06 (2H, d, *J* 17, 5-$H_n$ and 10-$H_n$), 4.22 (2H, s, 11-H), 4.57 (2H, d, *J* 17, 5-$H_x$ and 10-$H_x$), 10.01 (2H, s, CHO); $\delta_C$($CDCl_3$, 75 MHz) 11.4 ($CH_3$), 52.2 (C-5 and C-10), 68.1 (C-11), 134.4, 134.8, 142.0 (C-2 and C-7), 145.7 (C-3a and C-8a), 181.8 (CHO); *m*/*z* 318 ($M^+$, 100%), 290 (M − CO, 30), 257 (11), 67 (23), 45 (HCS, 31).

**2,7-Bis(1-hydroxy-1,1-diphenylmethyl)-4,5,9,10-tetrahydro-4,9-methanodithieno[3,2-*b*:3′,2′-*f*][1,5]diazocine 13.** Colorless needles (from methanol); mp 260–262 °C (Found: C, 74.5; H, 4.9; N, 4.8. $C_{37}H_{30}N_2O_2S_2$ requires C, 74.2; H, 5.05; N, 4.7%); $\nu_{max}$(KBr)/cm$^{-1}$ 3224 (OH), 3086, 3057, 3026, 2947, 2916, 2854, 1554, 1491, 1446, 1389, 1356; $\delta_H$(DMSO-$d_6$, 400 MHz) 3.85 (2H, d, *J* 16, 5-$H_n$ and 10-$H_n$), 4.08 (2H, s, 11-H), 4.35 (2H, d, *J* 16, 5-$H_x$ and 10-$H_x$), 6.42 (2H, s, 3-H and 8-H), 6.72 (2H, s, OH, disappeared by $D_2O$ addition), 7.20–7.32 (20H, m, Ph); $\delta_C$(DMSO-$d_6$, 100 MHz) 52.6 (C-5 and C-10), 66.9 (C-11), 78.5 (*C*(Ph)$_2$OH), 122.5, 126.8, 126.89, 126.93, 127.47, 127.51, 144.2, 146.8, 147.2, 149.4; *m*/*z* 598 ($M^+$, 100%), 581 (M − OH, 24), 570 (38), 415 (M − $Ph_2COH$, 21), 105 (60).

**(4*S**,9*S**)-2,7-Bis[(*R**)-1-hydroxy-1-phenylmethyl]-4,5,9,10-tetrahydro-4,9-methanodithieno[3,2-*b*:3′,2′-*f*][1,5]diazocine 14 or (4*R**,9*R**)-2,7-bis[(*R**)-1-hydroxy-1-phenylmethyl]-4,5,9,10-tetrahydro-4,9-methanodithieno[3,2-*b*:3′,2′-*f*][1,5]diazocine 15.** $R_f$ = 0.3 (silica gel, hexane–ethyl acetate 1 : 3); a white solid (from benzene–ethanol 100 : 1); mp 229–230 °C (Found: C, 67.5; H, 4.8; N, 6.4. $C_{25}H_{22}N_2O_2S_2$ requires C, 67.2; H, 5.0; N, 6.3%); $\nu$(KBr)/cm$^{-1}$ 3230 (OH), 3060, 3028, 2949, 2904, 2856, 1556, 1493, 1450, 1400, 1358, 1340; $\delta_H$($CDCl_3$, 300 MHz) 2.50 (2H, br s, OH), 3.96 (2H, d, *J* 16, 5-$H_n$ and 10-$H_n$), 4.07 (2H, s, 11-H), 4.39 (2H, d, *J* 16, 5-$H_x$ and 10-$H_x$), 5.91 (2H, s, C*H*(Ph)OH), 6.58 (2H, s, 3-H and 8-H), 7.30–7.43 (10H, m, Ph); $\delta_C$($CDCl_3$, 100 MHz) 53.3 (C-5 and C-10), 67.7 (C-11), 72.6 (*C*H(Ph)OH), 121.3 (C-3 and C-8), 123.3 (C-5a and C-10a), 126.2, 128.1, 128.6, 142.7, 144.5 (C-2 and C-7), 145.2 (C-3a and C-8a); *m*/*z* 446 ($M^+$, 100%), 418 (27), 339 (M − PhCHOH, 12), 105 (PhCO, 40), 77 (25).

**2-[(*R**)-1-Hydroxy-1-phenylmethyl]-7-[(*S**)-1-hydroxy-1-phenylmethyl]-4,5,9,10-tetrahydro-4,9-methanodithieno[3,2-*b*:3′,2′-*f*][1,5]diazocine 16.** $R_f$ = 0.2 (silica gel, hexane–ethyl acetate 1 : 3); colorless needles (from benzene–ethanol 100 : 1); mp 225–226 °C (Found: C, 67.3; H, 4.8; N, 6.4. $C_{25}H_{22}N_2O_2S_2$ requires C, 67.2; H, 5.0; N, 6.3%); $\nu_{max}$(KBr)/cm$^{-1}$ 3396 (OH), 3062, 3030, 2952, 2904, 2854, 1558, 1452, 1394; $\delta_H$($CDCl_3$, 300 MHz) 2.53 (2H, br s, OH), 3.94 (1H, d, *J* 16, 5-$H_n$ or 10-$H_n$), 3.95 (1H, d, *J* 16, 10-$H_n$ or 5-$H_n$), 4.06 (2H, s, 11-H), 4.37 (1H, d, *J* 16, 5-$H_x$ or 10-$H_x$), 4.40 (1H, d, *J* 16, 10-$H_x$ or 5-$H_x$), 5.89 (1H, s, C*H*(Ph)OH), 5.90 (1H, s, C*H*(Ph)OH), 6.55 (1H, s, 3-H or 8-H), 6.57 (1H, s, 8-H or 3-H), 7.28–7.43 (10H, m, Ph); $\delta_C$($CDCl_3$, 100 MHz) 53.3 (C-5 and C-10), 67.7 (C-11), 72.5 (*C*H(Ph)OH), 72.6 (*C*H(Ph)OH), 121.3 (C-3 or C-8), 121.4 (C-8 or C-3), 123.33 (C-5a or C-10a), 123.35 (C-10a or C-5a), 126.2, 126.3, 128.09, 128.14, 128.56, 128.58, 142.5, 142.7, 144.45 (C-2 or C-7), 144.56 (C-7 or C-2), 145.0 (C-3a or C-8a), 145.2 (C-8a or C-3a); *m*/*z* 446 ($M^+$, 100%), 418 (26), 339 (M − PhCHOH, 13), 105 (PhCO, 44), 77 (29).

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