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Generation and Cyclization of Thiocarbonyl *S*-Ylides by Reaction of Diazocompounds with *C*-Sulfonyldithioformates

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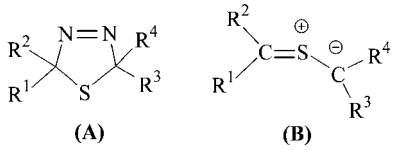
ABSTRACT: *The unexpected 1,3-benzodithiine derivatives* **5b,c** *were obtained from the reactions of trimethylsilyldiazomethane* **2** *with C-sulfonyldithioformates, bearing pentachlorophenylthio group,* **1b,c** *via unprecedented cyclization of the transient thiocarbonyl ylides* **4b,c**. *While the corresponding reaction with C-sulfonyldithioformates, bearing phenylthio group, afforded* **5a** *via [2 + 3]-cycloadditive dimerization of a transient thiocarbonyl ylides* **4a**. *Under the same reaction condition, C-sulfonyldithioformates* **1d–f** *react with diazomethane and/or phenyldiazomethane to afford the unsymmetrical 1,3-dithiolane* **7d,e** *and thiirane* **8e,f** *derivatives, respectively.* © 2007 Wiley Periodicals, Inc. Heteroatom Chem 18:28–33, 2007; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20246

INTRODUCTION

The reactions of thioketones with diazo compounds have been intensively studied [1–15]. It has been reported that thiocarbonyl compounds react very efficiently with diazo derivatives to give 2,5-dihydro-1,3,4-thiadiazoles of type **A** [7]. Most of these adducts **A** are rather unstable at ambient temperature and eliminate N_2 spontaneously or after slight warming they give reactive thiocarbonyl ylides of type **B**. These thiocarbonyl ylides can undergo various reactions, depending on the substitution pattern and/or on the reaction conditions, for example, 1,3-dipolar cycloadditions [4,8], ring closure to thiiranes [8–10], dimerization to 1,4-dithianes [11], 1,4-shifts [12], and 1,3- and 1,5-electrocyclizations [8,13].



These reactions between thiocarbonyl group and diazo compounds were also found useful for some preparative applications in the synthesis of several complex natural products, as representative examples of the use of thiocarbonyl ylides in natural product synthesis, the antibiotic indolizomycin [16,17], and the alkaloids chilenine and cephalotaxine [18]. In these cases, the formation of the corresponding thiocarbonyl ylides served as the key intermediates for the successful accomplishment of their total syntheses.

Our ongoing interest [15,19–23] in the organic chemistry of sulfur is focused on cycloaddition reactions of *C*-sulfonyldithioformates **1**, which constitute an interesting class of electron-depleted thiocarbonyl compounds. This class of *C*-sulfonylated thiocarbonyl compounds is also regarded as super-dipolarophiles [24]. In our recent work, we have shown that the reaction of **1** with

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trimethylsilyldiazomethane leads to the unprecedented [2 + 3]-cycloadditive dimerization of transient thiocarbonyl ylides [15]. This result prompted us to investigate the influence of the substituents on the reactivity of *C*-sulfonyldithioformates toward diazocompounds.

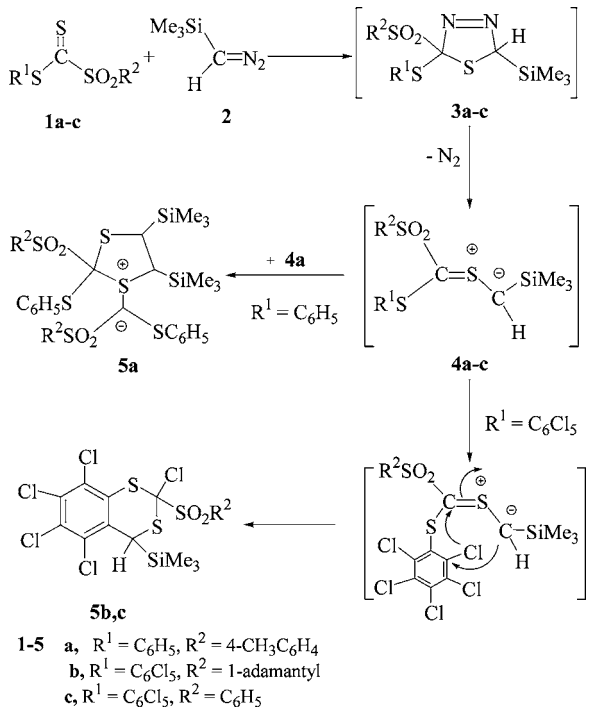
RESULTS AND DISCUSSION

The starting compounds, *C*-sulfonyldithioformates **1a–f**, were synthesized from the reaction of chlorodithioformates ClCSSR[1] with sulfinate anions $R^2SO_2^-$ in the presence of a phase transfer catalyst, according to our reported method [25]. In order to validate the reproducibility of our previously reported result [15], the reaction of **1a**, bearing phenylthio group, was easily performed in anhydrous tetrahydrofuran (THF) with trimethylsilyldiazomethane **2** at −78°C, followed by immediate warm up to room temperature to give the expected 1,3-dithiolanium derivative **5a** in excellent yield. NMR, mass spectra, and elemental analysis established the structure of **5a**. This was formed via [2 + 3]-cycloadditive dimerization of a transient thiocarbonyl ylide **4a**. ^{1}H NMR spectrum showed two doublets of signals at $\delta = 3.43$ and 3.54 ppm with $J = 13.2$ and 13.6 Hz, respectively, due to the two adjacent methine (CH) groups, while the two singlets at $\delta = 0.01$ and 0.44 ppm are assigned to the two nonequivalent trimethylsilyl groups. The NMR data of **5a** were in good agreement with the previously reported analogue [15] and were consistent with the formation of the cycloadduct of the type **5a**. However, the reaction of *C*-sulfonyldithioformates **1b**, bearing bulky substituents, with trimethylsilyldiazomethane **2** under the same condition afforded the unexpected 1,3-benzodithiine derivative **5b** in 85% yield. Interestingly, the absence of the two doublets in the ^{1}H NMR of **5b** as compared with **5a** and with the previously reported NMR data [15] confirmed that **4** behaved in a different manner when the phenyl moiety attached to the sulfur atom in **1a** was replaced by a pentachlorophenyl group.

We further performed an analogous reaction of **1c**, bearing only one bulky group, with trimethylsilyldiazomethane **2**; again, the NMR data of the resulting product **5c** are similar to its analogous **5b** which were obtained from **1b**. Based on the NMR analysis, mainly one single diastereomer was formed in a good yield and was identified as 1,3-benzodithiine derivatives **5b,c**. In addition to the structure elucidation of the 1,3-benzodithiine derivatives **5b,c** by the NMR, mass spectra, and elemental analysis, **5b** was subjected to an X-ray crystal structure analysis, which unambiguously confirmed the 1,3-benzodithiine structure (Fig. 1) [26].

It is still not clear what is the origin of the driving force for such type of intramolecular cyclization of the transient thiocarbonyl ylides **4b,c**. However, the formation of **5b,c** is most likely explained by subsequent intramolecular nucleophilic displacement of the chlorine atom located at the ortho-position of the pentachlorophenylthio group by the silyl-substituted negative carbon atom of thiocarbonyl ylides **4b,c**, followed by simultaneous attack of chloride anion on the carbocationic positive pole of **4b,c** affording the final products **5b,c** (Scheme 1).

In order to extend the scope of this intramolecular cyclization with the other nonsilylated diazoalkanes, we further investigated the analogous reaction of **1**, bearing pentachlorophenylthio group, with other diazoalkanes such as diazomethane and phenyldiazomethane [27]. Thus, an etheral solution of diazomethane was added to **1d,e** in dry solution of THF at −78°C, followed by warm up to room temperature to afford the unsymmetrical 1,3-dithiolanes **7d,e** and not the 1,3-benzodithiine derivatives **5b,c**. The regiochemistry of the unsymmetrical 1,3-dithiolane ring structures of **7d,e** can be deduced from the NMR spectra in which the two methyl groups are nonequivalent, and the CH_2 group gave a low-field shifted AB-system at $\delta = 3.57$, 3.89



SCHEME 1

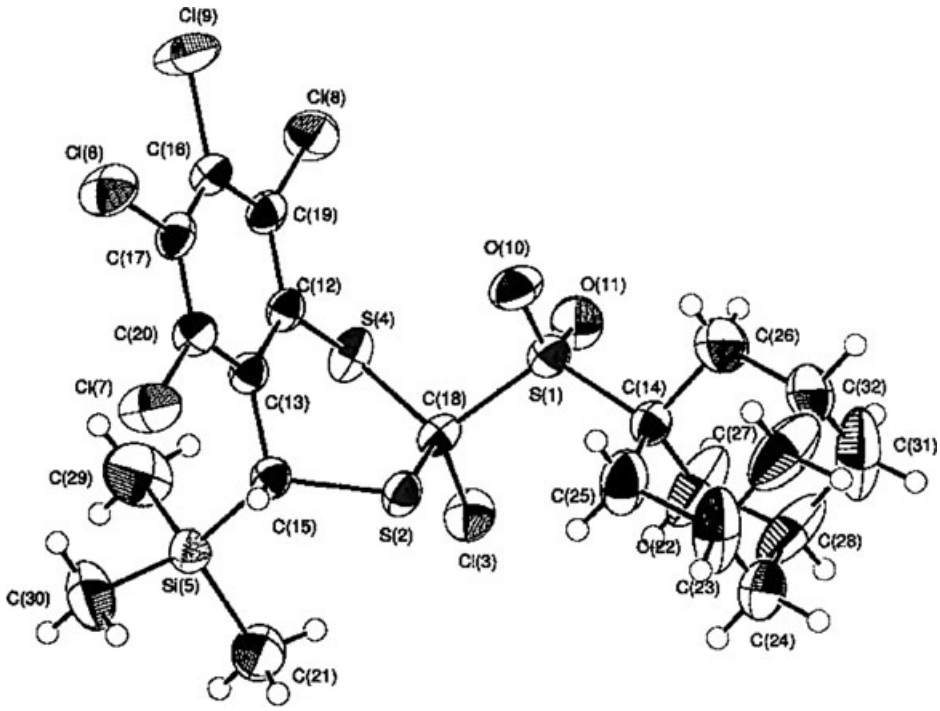
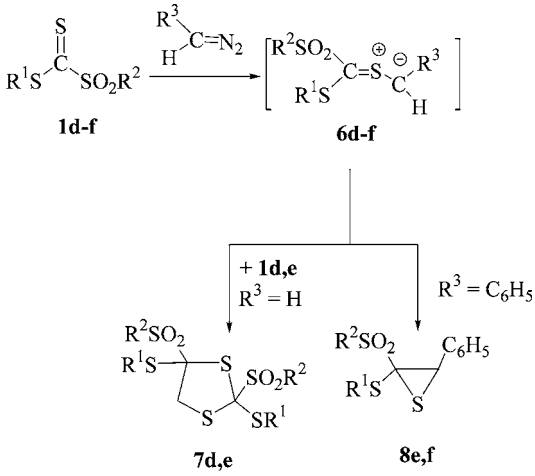


FIGURE 1 Crystal structure of 1,3-benzodithiine **5b** with 50% probability ellipsoids.

and 3.63, 3.94 ppm for **7d** and **7e**, respectively with $J_{AB} = 16$ Hz.

As a third diazo compound, phenyldiazomethane was tested in the reaction with **1e,f** in dry solution of THF at −78°C, followed by immediate warm up to room temperature and stirred till the red-colored solution of **1e,f** had disappeared to give thiiranes **8e,f**. The structural assignments of the crude **8e,f** by ^{1}H NMR analysis showed that only one regioisomer was formed, giving a singlet signal of one proton at $\delta = 4.07$ and 4.54 ppm assigned to thiirane ring proton for **8e** and **8f**, respectively and fall into the same range as in the reported shifts of the thiirane ring proton [10]. The key intermediate leading to thiiranes **8e**,**f** is again thiocarbonyl ylides **6e,f** resulting from immediate elimination of nitrogen from the initial cycloadduct 1,3,4-thiadiazole **A** and spontaneously cyclized to the corresponding stable thiiranes **8e,f**, and there is no evidence for the formation of the 1,3-benzodithiine structure (Scheme 2). Based on these results from the nonsilylated diazoalkanes, it seems likely that the presence of a chlorine atom at the ortho-position of the arylthio group in compatibility with the presence of trimethylsilyl group with diazo alkanes is indispensable for the intramolecular cyclization of the in situ generated thiocarbonyl ylides. Attempts to trap the intermediate thiocarbonyl ylides **4** and **6** with the alkenic and alkynic dipolarophiles



SCHEME 2

were unsuccessful; dimerization or intramolecular cyclization was the preferred reaction pathway.

In conclusion, we have shown that the reactivity of the in situ generated silyl-substituted thiocarbonyl ylides depends on the substituents at the thiocarbonyl carbon atom of **1**. The study also confirmed that the cyclization of the transient thiocarbonyl ylides derived from diazomethane and

phenyldiazomethane with **1** is not similar to that observed in the case of trimethylsilyldiazomethane.

EXPERIMENTAL

All ^{1}H and ^{13}C NMR experiments ($CDCl_3$) were carried out with a Varian Unity 400 MHz spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C). Chemical shifts are reported in ppm relative to TMS using appropriate solvent signals as internal standard. Mass spectra analysis was performed with a Kratos 50 TC spectrometer, and ES mass spectra were obtained on a Bruker Esquire 3000 plus mass spectrometer. Melting points were recorded on a Büchi melting point apparatus and are uncorrected. Solvents were dried/purified according to literature procedures. Single crystals suitable for X-ray studies from **5b** were grown in a mixture of CH_2Cl_2 and *n*-hexane (1:3); X-ray calculations were performed using maXus (Bruker Nonius, Delft and MaxScience, Japan).

2-Phenylthio-2-(p-tolylsulfonyl)-4,5-bis(trimethylsilyl)-1,3-dithiolan-1-ium(4-chlorophenylthio)(phenylsulfonyl)methylide **5a**

Trimethylsilyldiazomethane **2** [28] (2 M in hexane solution, 0.50 mL, 1 mmol) was added dropwise to a stirred solution of **1a** (250 mg, 0.81 mmol) in 15 mL of dry THF under nitrogen at −78°C. The reaction mixture was allowed to warm up to room temperature over 1 h, after some time the red color of **1a** disappeared. Evaporation of the solvents under reduced pressure left a colorless solid residue, which was recrystallized from diethyl ether/hexane (3:1) to give **5a** (290 mg, 91% yield) as a colorless crystals, mp 138–139°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.01 (s, 9H), 0.44 (s, 9H), 2.35 (s, 3H), 2.66 (s, 3H), 3.43 (d, $J = 13.2$ Hz, 1H), 3.54 (d, $J = 13.6$ Hz, 1H), 7.02 (d, $J = 8$ Hz, 2H), 7.17–7.68 (m, 14H), 8.18 (d, $J = 8$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ −1.26, 0.08, 21.48, 21.88, 41.11, 57.93, 61.09, 107.92, 125.66, 126.24, 127.27, 128.15, 128.70, 129.51, 129.70, 130.49, 132.29, 132.94, 136.46, 141.31, 141.46, 142.40, 146.02 ppm; MS (ESI): *m/z* 811 ($M^+ + Na$, 18%). Anal. Calcd. for $C_{36}H_{44}O_4S_6Si_2$ (789.30): C, 54.78; H, 5.62; S, 24.38. Found: C, 54.37; H, 5.58; S, 23.92.

2-Chloro-2-(1-adamantylsulfonyl)-4-trimethylsilyl-5,6,7,8-tetrachloro-1,3-benzodithiine **5b**

The procedure as given for **5a** was followed starting from **1b** (350 mg, 0.67 mmol) and trimethylsilyldiazomethane (0.40 mL, 0.8 mmol). The crude product was purified by crystallization (CH_2Cl_2/*n*-hexane = 1:3) to give **5b** as a colorless crystal (347 mg, 85% yield), mp 143–145°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.19 (s, 9H), 1.73–1.79 (br m, 6H), 2.21 (br s, 6H), 2.40 (br s, 3H), 4.32 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 1.14, 28.69, 35.68, 38.26, 63.73, 72.87, 102.70, 130.70, 132.94, 133.53, 139.17, 142.21, 142.81 ppm; MS (ESI): *m/z* 400 [$(M^+ + 1,\ 25\%) - C_{13}H_{24}Si$]. Anal. Calcd. for $C_{21}H_{25}Cl_5O_2S_3Si$ (610.97): C, 41.28; H, 4.12; S, 15.75. Found: C, 40.17; H, 4.38; S, 15.32.

2-Chloro-2-phenylsulfonyl-4-trimethylsilyl-5,6,7, 8-tetrachloro-1,3-benzodithiine **5c**

The procedure as given for **5a** was followed starting from **1c** (300 mg, 0.64 mmol) and trimethylsilyldiazomethane (0.40 mL, 0.8 mmol). The crude product was purified by crystallization (CH_2Cl_2/*n*-hexane = 1:3) to give **5c** as a colorless crystal (290 mg, 82% yield), mp 167–169°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.49 (s, 9H), 4.22 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 0.40, 65.86, 103.52, 128.23, 128.44, 128.76, 128.85, 131.79, 132.67, 138.38, 134.75, 135.01, 135.68 ppm; MS (ESI): *m/z*400 [$(M^+ + 1) - C_9H_{14}Si$, 35%]. Anal. Calcd. for $C_{17}H_{15}Cl_5O_2S_3Si$ (552.85): C, 36.89; H, 2.71; S, 17.36. Found: C, 37.17; H, 2.58; S, 16.98.

2,5-Bis(phenylsulfonyl)-2,5-bis(p-tolylthio)-1,3-dithiolane **7d**

Freshly prepared solution of diazomethane [29] (2 mL, 1.40 equiv.) was added under nitrogen in a small quantity to a stirred solution of **1d** (300 mg, 0.97 mmol) in 10 mL of dry THF at −78°C. The reaction mixture was allowed to warm up to room temperature over 1 h, after which time the red color of **1d** disappeared. Nitrogen was bubbled through the solution followed by evaporation of the solvents under reduced pressure to give a colorless solid residue, which was recrystallized from diethyl ether/hexane to give a colorless crystal of **7d**. Yield 280 mg (92%), mp 156–157°C. ^{1}H NMR ($CDCl_3$): δ 2.35 (s, 3H), 2.38 (s, 3H), 3.57 (d, $J = 16$ Hz, 1H), 3.89 (d, $J = 16$ Hz, 1H), 7.15 (m, 4H), 7.59 (m, 10H), 7.92 (d, 2H, $J = 8.00$ Hz), 8.04 (d, 2H, $J = 8.00$ Hz); ^{13}C NMR ($CDCl_3$) δ 21.38, 21.46, 44.11, 44.88, 96.62, 96.99, 128.19, 128.66, 129.38, 129.66, 129.76, 131.83, 132.73, 134.11, 135.23, 137.60, 137.97, 138.84, 141.16, 141.26, 141.35, 141.61 ppm; MS: 348 ($M - 2C_6H_5SO_2$, 68%). Anal. Calcd. for $C_{29}H_{26}O_4S_6$ (630.91): C, 55.21; H, 4.15; S, 30.49. Found: C, 55.46; H, 4.44; S, 29.22.

2,5-Bis(pentachlorophenylthio)-2,5-bis(p-tolylsulfonyl)-1,3-dithiolane **7e**

The procedure as given for **7d** was followed starting from **1e** (300 mg, 0.62 mmol) and diazomethane (ca. 1.4 equiv.). The crude product was purified by crystallization (CH_2Cl_2/*n*-hexane = 1:3) to give **7e** as a colorless crystal. Yield 270 mg (89%), mp 221–222°C. ^{1}H NMR ($CDCl_3$): δ 2.38 (s, 3H), 2.42 (s, 3H), 3.63 (d, $J = 16$ Hz, 1H), 3.94 (d, $J = 16$ Hz, 1H), 7.83 (m, 4H), 8.09 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 21.43, 21.52, 44.31, 44.92, 96.72, 97.09, 128.07, 128.90, 129.45, 129.77, 131.84, 132.62, 134.21, 135.38, 137.97, 138.84, 141.16, 141.35, 142.73, 143.05, 144.87, 145.80 ppm; MS: 970 (M^+, 46%). Anal. Calcd. for $C_{29}H_{16}Cl_{10}O_4S_6$ (975.35): C, 35.71; H, 1.35; S, 19.73%. Found: C, 35.89; H, 1.71; S, 19.64.

2-Pentachlorophenylthio-2-(p-tolylsulfonyl)-3-phenylthiirane **8e**

To a solution of **1e** (300 mg, 0.62 mmol) in dry THF (10 mL), freshly prepared solution of phenyldiazomethane [30] was added under nitrogen in dry diethylether (5 mL, 1.5 equiv.) at −78°C. The reaction mixture was immediately warmed to room temperature and stirred till the red-colored solution turned colorless (20 min). The solvent was evaporated under reduced pressure to give a white residue, which was twice recrystallized from CH_2Cl_2/*n*-hexane (1:3) to give a colorless crystal of **8e**. Yield 310 mg (88%), mp 124–126°C. ^{1}H NMR ($CDCl_3$): δ 2.42 (s, 3H), 4.07 (s, 1H), 7.16 (d, 3H, $J = 8.00$ Hz), 7.37 (m, 7H); ^{13}C NMR ($CDCl_3$): δ 21.71, 49.10, 73.95, 127.93, 128.55, 129.10, 129.41, 129.85, 130.33, 130.53, 132.61, 134.05, 136.90, 140.97, 145.40 ppm; MS: *m/z* 536 ($M^+ - S$, 29%). Anal. Calcd. for $C_{21}H_{13}Cl_5O_2S_3$ (570.79): C, 44.19; H, 2.30; S, 16.85. Found: C, 44.39; H, 2.51; S, 16.64

2-(4-Chlorophenylthio)-2-(4-chlorophenylsulfonyl)-3-phenylthiirane **8f**

The procedure as given for **8e** was followed starting from **1f** (300 mg, 0.82 mmol) and phenyldiazomethane (ca. 1.4 equiv.). The crude product was purified by crystallization (diethylether/*n*-hexane = 1:3) to give **8f** as a colorless crystal. Yield 320 mg (86%), mp 112–115°C. ^{1}H NMR ($CDCl_3$): δ 4.54 (s, 1H), 7.25 (m, 9H), 7.38 (d, $J = 8$ Hz, 2H), 7.63 (d, $J = 8$ Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 54.00, 73.90, 127.97, 128.52, 128.77, 129.30, 130.07, 130.09, 130.16, 131.67, 135.26, 136.21, 136.50, 140.63 ppm; MS: *m/z* 420 ($M^+ - S$, 23%). Anal. Calcd. for $C_{20}H_{14}Cl_2O_2S_3$ (453.43): C, 52.98; H, 3.11; S, 21.12. Found: C, 53.09; H, 2.91; S, 20.84.

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[26] Crystal data for **5b** Mo Kα radiation: $\lambda = 0.71073$ Å; cell measurement temperature: 298 K; crystal color: colorless; crystal system: monoclinic; unit

cell parameters: $a = 15.8644(5)$ Å, $b = 12.9199(4)$ Å, $c = 13.0313(1)$ Å, $\alpha = 90.00°$, $\beta = 96.0113°$ (12)°, $\gamma = 90.00°$; space group: $P2_1/c$; cell volume: 2656.29(14) Å^3; R_{all}: 0.110; cell formula units Z: 4. Complete X-ray data for compound **5b** was deposited at the Cambridge Crystallographic Data Center under the reference number CCDC 254756, copies of the data can be obtained free of charge on application to: CCDC, 12 Union Road, Cambridge CB2 IEZ, UK (Fax: +44-1223-336033 or E-mail: deposit@ccdc.cam.ac.uk).

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