

A novel thiopyran-4-thione synthesis and crystal structure of a thiopyran-4-thione

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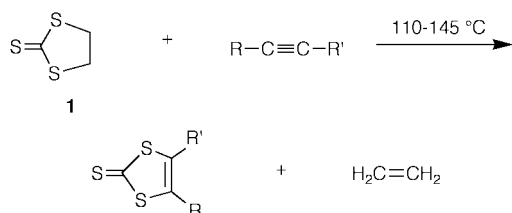
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The zinc(II) chloride catalysed reaction between ethylene trithiocarbonate (**1**) and dibenzoylacetylene (**3**) gave the novel 2,3,5,6-tetrabenzoylthiopyran-4-thione (**4a**) and its structure was elucidated by X-ray crystallography. Treatment of 2,3,5,6-tetrabenzoylthiopyran-4-chalcogenones (**4a,b**) with triethyl phosphite afforded the bis-annelated furans 1,3,5,7-tetraphenylthiopyrano[2,3-*c*:5,6-*c'*]difuran-8-chalcogenones (**5a,b**) in almost quantitative yields. The mechanism for this furan formation is discussed.

Introduction

Several alkynes having electron-withdrawing groups react smoothly with ethylene trithiocarbonate (**1**) to give substituted 1,3-dithiole-2-thiones **2** in good to moderate yields (Scheme 1).¹



- 2a** R, R' = CF₃, 76% (ref. 1a)
2b R, R' = COOMe, 70% (ref. 1a, b)
2c R = CHO; R' = CH(OEt)₂, 60% (ref. 1c)
2d R = COOMe; R' = H, 40% (ref. 1d)
2e R = CN; R' = H, 33% (ref. 1b)
2f R, R' = H, 2-5% (ref. 1b)

Scheme 1

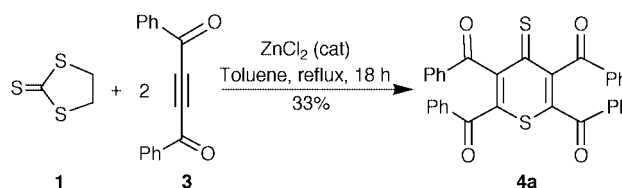
The reaction proceeds as a cycloaddition between the alkyne and ethylene trithiocarbonate (**1**) resulting in ethylene evolution. However, acetylene (case **2f**) reacts only under forcing conditions, and ethylene trithiocarbonate (**1**) does not react with methyl-, phenyl- or diphenylacetylenes.^{1b} The scope of the reaction appears to be limited to alkynes containing electron-withdrawing substituents.

We present here the first synthesis of a thiopyran-4-thione derivative from ethylene trithiocarbonate (**1**) and an alkyne together with the first crystal structure of a thiopyran-4-thione.² The trialkyl phosphite assisted cyclisation of 1,4-dioxoalkenes to furans has, to our knowledge, only been sporadically described in the literature.³ During this work we found that the method works well for 2,3,5,6-tetrabenzoylthiopyran-4-chalcogenones.

Results and discussion

From the results depicted in Scheme 1 it would have been expected that dibenzoylacetylene (**3**)⁴ would react with ethylene trithiocarbonate (**1**) to give 4,5-dibenzoyl-1,3-dithiole-2-thione. Although several attempts were made and different solvents were tried, we never succeeded in obtaining 4,5-dibenzoyl-1,3-dithiole-2-thione by this route.⁵

Refluxing a catalytic amount of zinc(II) chloride and a 1:1 mixture of ethylene trithiocarbonate (**1**) and dibenzoylacetylene (**3**) in toluene for 18 h gave a different result. Work-up by column chromatography afforded the novel 2,3,5,6-tetrabenzoylthiopyran-4-thione (**4a**) as a green solid (Scheme 2).⁶ †



Scheme 2

¹H NMR, ¹³C NMR, high resolution mass spectrometry and microanalysis all supported the proposed structure **4a**. Furthermore, the structure of the thiopyran-4-thione product was unequivocally determined by single crystal X-ray structure analysis. Single crystals (green needles) of **4a** were obtained by slow evaporation of an acetone solution of **4a**. Fig. 1 shows the molecular structure of **4a**. The molecule has an apparent inversion center in the crystal structure. Thus each molecule appears to be superimposed by its inverted counterpart, although the inversion center is not dictated by crystal symmetry. An explanation might be that during crystallisation each molecule adopts one of two orientations (thione up or down) which, however, has little effect on the conformation of the benzoyl groups and the packing of the molecules. This disorder was modeled by having S1, S2 and C33 partly (50%) allocated to their inversion-related positions S1A, S2A and C33A, which led to a satisfactory refinement of the structure when the disordered parts were restrained to be almost identical. Therefore, the calculated distances and angles involving these atoms should be interpreted with caution. Apparent highly anisotropic displacements of O2 and O4 were modeled by split atom positions for these atoms (50/50%). No other crystal structure of a thiopyran-4-thione has been reported in the Cambridge Crystallographic Database.⁷

The optimum yield of **4a** was obtained by using a 1:1 mixture of ethylene trithiocarbonate (**1**), dibenzoylacetylene (**3**)

† Employing a 1:2 mixture of **1** and **3** did not increase the yield of **4a**. It was unfortunately not possible to characterise any other products unambiguously from the reaction mixture.

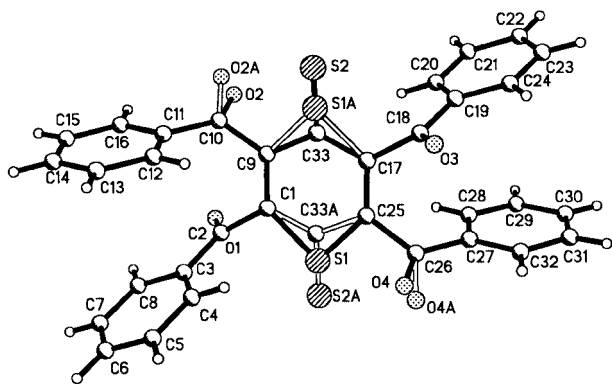
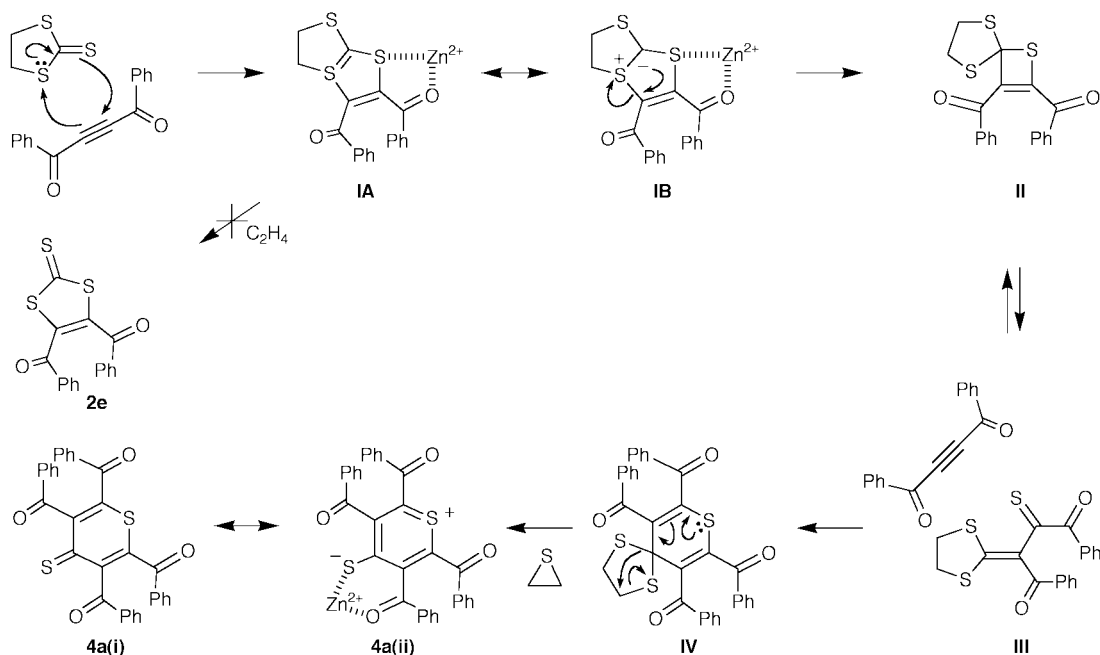


Fig. 1 Molecular structure of **4a**. S1A, S2A, C33A, O2A and O4A are alternate positions for S1, S2, C33, O2 and O4, *cf.* discussion of disorder in text.

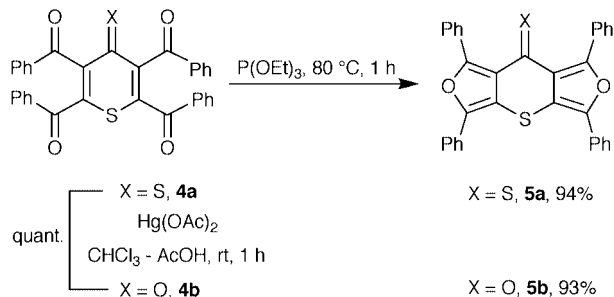
and 15 mol% zinc(II) chloride. Employing 100 mol% zinc(II) chloride did not increase the yield of **4a**, hence zinc(II) chloride probably acts as a catalyst for the reaction. A possible route for the formation of **4a** from **1** and **3**, shown in Scheme 3, involves a 1,3-dipolar cycloaddition of ethylene trithiocarbonate (**1**) on dibenzoylacetylene (**3**) to give the intermediate **IA**↔**IB**. For the alkynes shown in Scheme 1 this type of intermediate loses ethylene to give 1,3-dithiole-2-thiones. Instead, **IB** rearranges to the spiro-thiete compound **II** facilitated by the positively charged sulfur atom and coordination of zinc(II) to a carbonyl group and a sulfur atom, which makes the olefinic carbon next to the positively charged sulfur extremely electrophilic. Conversion of **II** to the vinylog 1,3-dithiolane-2-thione **III**,⁸ followed by a [4 + 2] cycloaddition of **III** and dibenzoylacetylene gives the dithioketal **IV**.⁹ Using plasma desorption mass spectrometry a species with *m/z* 604 was detected in the reaction mixture, which could be assigned to the dithioketal **IV**. Finally, **IV** loses thiirane to give the dipolar form **4a(ii)** of **4a**.[‡]

[‡] Refluxing a 1 : 1 mixture of ethylene trithiocarbonate (**1**) and dimethyl acetylenedicarboxylate and 15 mol% zinc(II) chloride in toluene afforded exclusively 4,5-bis(methoxycarbonyl)-1,3-dithiole-2-thione (**2b**). It is not fully understood why these reagents exclusively give **2b**. An explanation could be the fundamental difference in reactivity between an ester group and a keto group together with competition between the different reaction pathways.



Scheme 3

Transchalcogenation of thione **4a** using mercuric acetate in a mixture of chloroform and glacial acetic acid gave the corresponding ketone **4b** as a colourless solid in quantitative yield (Scheme 4).¹⁰ Treatment of **4a,b** with triethyl phosphite followed by addition of methanol to the reaction mixture and filtration afforded the bis-annulated furans **5a,b** in almost quantitative yields as orange and brown solids, respectively (Scheme 4). Elemental analyses and spectral data for compounds **5a,b** were all consistent with the assigned structures.



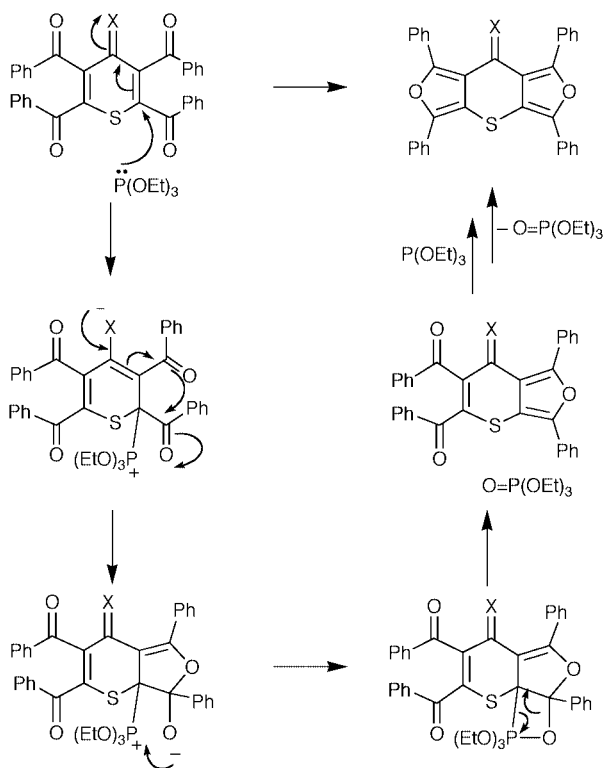
Scheme 4

The difference between the thiopyran-4-thione **4a** and the thiopyran-4-one **4b** is easily seen from their IR spectra. In both spectra a broad absorption band ($\nu = 1668 \text{ cm}^{-1}$ in **4a** and $\nu = 1669 \text{ cm}^{-1}$ in **4b**) is seen emanating from the carbonyl stretching mode in the benzoyl groups, but in the spectrum of **4b** an additional carbonyl stretching band ($\nu = 1609 \text{ cm}^{-1}$) from the thiopyran-4-one nucleus is observed. In the IR spectra of **5a,b** the broad benzoyl carbonyl absorption band is absent. The carbonyl absorption band from the thiopyran-4-one nucleus in **5b** is shifted (45 cm^{-1}) towards a higher frequency ($\nu = 1654 \text{ cm}^{-1}$) compared to the carbonyl absorption band in the thiopyran-4-one nucleus of **4b**, indicating that the carbon-oxygen bond in the thiopyran-4-one nucleus of **5b** has more double bond character as compared to its counterpart in **4b**.

§ In the parent thiopyran-4-one the carbonyl stretching band is observed at 1609 cm^{-1} (br) (ref. 11). The lack of any absorption band in the 1660 cm^{-1} region, which would be expected for a conjugated carbonyl group, indicates that the thiopyran-4-one nucleus is a resonance hybrid containing small or no contributions from forms with a carbon-oxygen double bond (ref. 11).

Finally, a carbonyl absorption band is absent from the IR spectrum of **5a**, which is consistent with the assigned structure.

Conversion of **4a,b** to **5a,b**, by treatment with triethyl phosphite, is formally a reduction. A likely reaction mechanism for the formation of **4a,b** from **5a,b** is shown in Scheme 5. The first



Scheme 5

step is a nucleophilic attack of triethyl phosphite at the C-2 position in the thiopyran-4-chalcogenone in a Michael fashion.[¶] In the next step the five-membered ring is formed by attack of the partly negatively (by delocalization) charged oxygen atom on a neighbouring electrophilic benzoyl group giving a Wittig related intermediate. This betaine finally loses triethyl phosphate to give the aromatic furan ring. The driving force for this reaction is obviously the formation of two aromatic furan systems together with the formation of triethyl phosphite.

Conclusion

In conclusion, novel thiopyran-4-chalcogenones have been synthesised and characterised. The zinc(II) chloride catalysed formation of thiopyran-4-thiones from ethylene trithiocarbonate and alkynes have not previously been reported in the literature and further investigations of this new type of reaction are currently in progress. The unknown fused difurothiopyran-4-chalcogenones **5a,b** have been synthesised in high yields.

Experimental

All reactions were carried out under an atmosphere of dry nitrogen. Toluene was distilled from sodium–benzophenone. All reagents were standard grade and used as received unless otherwise stated. Analytical thin layer chromatography (TLC) was performed on Merck DC-Alufolien Kieselgel 60 F₂₅₄ 0.2 mm thickness precoated TLC plates, while column chromatography was performed using Merck Kieselgel 60 (0.040–0.063 mm, 230–400 mesh AST0000M). Melting points (mp)

[¶] The C-2 position in thiopyran-4-chalcogenones is normally the site of reaction with nucleophiles (ref. 2b).

were determined on a Büchi melting point apparatus and are uncorrected. ¹H NMR spectra were recorded on a Gemini-300BB instrument at 300 MHz, using the deuterated solvent as lock and TMS or the residual solvent as internal standard. *J* values are given in Hz. ¹³C NMR spectra were recorded at 75 MHz using broad band decoupling. Electron impact ionisation mass spectrometry (EIMS) was performed on a Varian MAT 311A instrument. Infrared (IR) spectra were recorded on a Perkin-Elmer 580 spectrophotometer. Microanalyses were performed at the Atlantic Microlab, inc., Atlanta, Georgia.

2,3,5,6-Tetrabenzoylthiopyran-4-thione **4a**

Ethylene trithiocarbonate (**1**) (1.36 g, 10.0 mmol) was dissolved in toluene (40 mL) whereupon the yellow solution was purged with nitrogen (10 min) before dibenzoylacetylene (**3**)² (2.34 g, 10.0 mmol) and anhydrous zinc(II) chloride (0.20 g, 1.5 mmol) were added. The mixture was refluxed for 18 h causing a slow colour change to dark green. After cooling to room temp., the solvent was removed *in vacuo* and the dark green oil was purified by column chromatography on silica using dichloromethane–cyclohexane (4:1) as eluent. The dark green band (*R_f* 0.3) was collected and concentrated to give the thiopyran-4-thione **4a** (0.89 g, 33%) as an analytically pure green solid; recrystallisation from toluene–cyclohexane gave **4a** (0.68 g, 25%) as green needles; mp 233.5–234 °C (Found: C, 72.89; H, 3.63; S, 11.70. C₃₃H₂₀O₄S₂ requires C, 72.78; H, 3.70; S, 11.77%); ν_{\max} (KBr)/cm⁻¹ 3060w, 1668s (br, PhCO), 1595s, 1580m, 1536m, 1449m, 1340w, 1316m, 1245s (br) and 1179m; δ_{H} (CDCl₃) 7.41 (4 H, t, *J* 7.5), 7.46 (4 H, t, *J* 7.6), 7.54 (2 H, t, *J* 7.3), 7.62 (2 H, t, *J* 7.4), 7.84 (4 H, d, *J* 7.4) and 7.89 (4 H, d, *J* 7.4 Hz); δ_{C} (CDCl₃) 128.75, 128.98, 129.09, 130.52, 133.86, 134.18, 135.36, 135.63 (Ar C), 138.14, 150.95 (C=C), 189.74, 192.65 (C=O) and 219.78 (C=S); *m/z* (EI) 544 (M⁺, 42%), 411 (17), 105 (100, PhCO⁺) and 77 (65) (Found: M⁺, 544.0800. C₃₃H₂₀O₄S₂ requires *M*, 544.0803).

Preparation of single crystals for X-ray analysis

Recrystallised **4a** (~5 mg) was dissolved in acetone (*ca.* 2 mL) and filtered through a folded filter paper in such a way that the filtrate directly went into a test tube (bore *ca.* 1 cm). The test tube was sealed with a septum, which was punctured with a short disposable needle, and allowed to stand in the dark. During one week green needles started to grow from the side and the bottom of the test tube.

2,3,5,6-Tetrabenzoylthiopyran-4-one **4b**

Mercuric acetate (0.80 g, 2.51 mmol) was added in one portion to a solution of **4a** (0.55 g, 1.01 mmol) in a mixture of chloroform (30 mL) and glacial acetic acid (3 mL) causing the initially green solution to change to white within 1 min. The resulting white suspension was stirred for 1 h at room temp., whereupon the white precipitate was filtered using Celite (1.0 cm) and washed thoroughly with dichloromethane (4 × 40 mL). The combined organic phase was washed with saturated aqueous sodium hydrogen carbonate (3 × 150 mL), water (2 × 150 mL) and dried over anhydrous magnesium sulfate. Evaporation of the solvent *in vacuo* afforded the thiopyran-4-one **4b** (0.53 g, quantitative) as an analytically pure off-white solid; mp 253–253.5 °C (from toluene–cyclohexane) (Found: C, 75.12; H, 3.90; S, 6.00. C₃₃H₂₀O₅S requires C, 74.99; H, 3.87; S, 6.07%); ν_{\max} (KBr)/cm⁻¹ 3061w, 1669s (br, PhCO), 1609s (br, CO in thiopyran unit), 1596s, 1580m, 1531w, 1449m, 1342m, 1315m, 1244s (br) and 1179w; δ_{H} (CDCl₃) 7.37–7.45 (8 H, m), 7.54 (2 H, t, *J* 7.4), 7.60 (2 H, t, *J* 7.4), 7.77 (4 H, d, *J* 7.3), 7.86 (4 H, d, *J* 7.3); δ_{C} (CDCl₃) 128.60, 128.88, 129.22, 130.32, 134.00, 134.05, 135.22, 135.90 (Ar C), 142.00, 149.27 (C=C), 176.82, 189.12 and 192.34 (C=O); *m/z* (EI) 528 (M⁺, 61%), 395 (18),

105 (100, PhCO⁺) and 77 (57) (Found: M⁺, 528.1012. C₃₃H₂₀O₅S requires M, 528.1031).

1,3,5,7-Tetraphenylthiopyrano[2,3-c:5,6-c']difuran-8-thione 5a

Compound **4a** (0.27 g, 0.50 mmol) was suspended in distilled triethyl phosphite (20 mL) and heated to 80 °C giving a brown precipitate. The brown suspension was stirred for 1 h at 80 °C, cooled to room temp., and addition of methanol (50 mL) yielded a brown solid which was filtered and washed with methanol (2 × 25 mL) to give the *thiopyran-8-thione* **5a** (0.24 g, 94%) as an analytically pure brown solid; mp >265 °C (Found: C, 77.44; H, 3.78; S, 12.54. C₃₃H₂₀O₂S₂ requires C, 77.32; H, 3.93; S, 12.51%); $\nu_{\max}(\text{KBr})/\text{cm}^{-1}$ 3058w, 1603m, 1583w, 1556m, 1531m, 1489m, 1476s, 1444m, 1382m, 1364w, 1178w, 1134m; $\delta_{\text{H}}(\text{CDCl}_3)$ 7.33–7.55 (12 H, m) and 7.83–7.87 (8 H, m); m/z (EI) 512 (M⁺, 66%), 511 (M⁺ – H, 100), 256 (17), 105 (17, PhCO⁺) and 77 (23) (Found: M⁺ – H, 511.0849. C₃₃H₁₉O₂S₂ requires M – H, 511.0827).

1,3,5,7-Tetraphenylthiopyrano[2,3-c:5,6-c']difuran-8-one 5b

Compound **4b** (0.53 g, 1.00 mmol) was suspended in distilled triethyl phosphite (40 mL) under nitrogen and heated to 80 °C giving an orange precipitate. The orange suspension was stirred for 1 h at 80 °C, cooled to room temp., and addition of methanol (100 mL) yielded an orange solid which was filtered and washed with methanol (2 × 50 mL) to give the *thiopyran-8-one* **5b** (0.46 g, 93%) as analytically pure orange needles; mp > 265 °C (Found: C, 79.54; H, 4.01; S, 6.53. C₃₃H₂₀O₃S requires C, 79.82; H, 4.06; S, 6.46%); $\nu_{\max}(\text{KBr})/\text{cm}^{-1}$ 3060w, 1654s (CO in thiopyran unit), 1602m, 1577m, 1557s, 1491m, 1479s, 1444m, 1374w; $\delta_{\text{H}}(\text{CDCl}_3)$ 7.36–7.58 (12 H, m), 7.89 (4 H, dd, *J* 8.5 and 1.1) and 8.26 (4 H, dd, *J* 8.0 and 1.6); m/z (EI) 496 (M⁺, 100%), 391 (8), 248 (25), 145 (55), 105 (73, PhCO⁺) and 77 (61) (Found: M⁺, 496.1125. C₃₃H₂₀O₃S requires M, 496.1132).

Crystallographic data for compound 4a ||

C₃₃H₂₀O₄S₂, *M* = 544.63, orthorhombic, *a* = 21.094(2), *b* = 5.6478(6), *c* = 21.496(2) Å, *V* = 2561.0(4) Å³, space group *Pca*2₁ (No. 29), *Z* = 4, *D_x* = 1.413 g cm⁻³, *F*(000) = 1128, graphite monochromated Mo-K α radiation, λ = 0.71073 Å, μ = 0.248 mm⁻¹, *T* = 120 K. Crystal size: 0.48 × 0.23 × 0.11 mm, green needles. The intensities of 25516 reflections were measured on a Siemens SMART CCD diffractometer to θ_{\max} = 26.40°, and were merged to 5235 unique reflections (*R*_{int} = 0.028). Structure solution, refinement and analysis of the structure, and production of crystallographic illustrations were carried out using the programs SHELXS97,^{12a} SHELXL97,^{12b} PLATON^{12c} and SHELXTL.^{12d} The refinement using 381 parameters converged at *R*₁ = 0.0362 (for *F*_o > 4 σ (*F*_o)).

|| CCDC reference number 207/404. See <http://www.rsc.org/suppdata/p1/a9/a908068f> for crystallographic files in .cif format.

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