Reaction of furans with trithiazyl trichloride: a new synthesis of isothiazoles

Xiao-Lan Duan, Ross Perrins and Charles W. Rees

Department of Chemistry, Imperial College of Science, Technology and Medicine, London, UK SW7 2AY

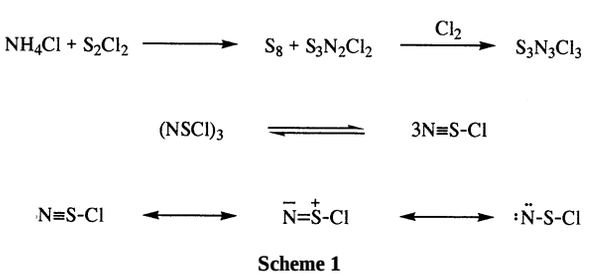
Trithiazyl trichloride 1 converts 2,5-diphenylfuran into 5-benzoyl-3-phenylisothiazole 2 regiospecifically and in high yield. This is a new ring opening of furans and a new synthesis of isothiazoles. 2,5-Bis(4-methylphenyl)furan, 3-bromo-2,5-diphenylfuran, 2,3,5-triphenylfuran, 2,5-di-*tert*-butylfuran and its 3-chloro and 3-bromo derivatives react in an entirely analogous manner to give the corresponding isothiazoles (55–85%) in synthetically useful, one-pot, conversions. 2,5-Diphenylthiophene reacts more slowly with the trimer 1 to give the same product, 2, as the corresponding furan, probably by oxidation of the analogous thiobenzoyl compound by the reagent, which is shown to oxidise thiobenzophenone to benzophenone very rapidly. Tetraphenylcyclopentadienone 8 reacts rapidly with the trimer to give 3,4,5,6-tetraphenyl-2(1*H*)-pyridone 10 (56%). Possible mechanisms in which the monomer, Cl–S≡N, is the reacting species are proposed for all of these reactions.

Introduction

In this and later papers we show that trithiazyl trichloride **1** reacts very readily with a wide range of simple organic substrates and is useful for the synthesis of organic sulfur–nitrogen compounds, particularly heterocyclic rings with N–S, N–S–N and S–N–S units. Some of our earlier work has been summarised.[1,2] Trithiazyl trichloride[3] is a stable, but moisture-sensitive, yellow crystalline solid which is prepared by heating ammonium chloride with disulfur dichloride, followed by chlorination of the initially formed salt, $S_3N_2Cl^+Cl^-$ (Scheme 1). Its six-membered ring has a slightly flattened chair conformation with all three chlorines axial and on the same side of the ring, the other side being exposed to nucleophilic attack and cycloadditions. The ring bonds are delocalised and all of equal length. The cyclic species (the 'trimer') **1** is in thermal equilibrium with the monomer, thiazyl chloride, N≡S–Cl, and on heating in inert solvents to about 60 °C the monomer imparts a characteristic green colour to the solution.[3] Various canonical forms (Scheme 1) can be written for thiazyl chloride which is highly reactive. The inorganic chemistry of trithiazyl trichloride has been extensively developed but its applications in organic synthesis are rare,[4] partly because its known reactions are often complex and low yielding, and their scope and mechanisms have not been established.

Trithiazyl trichloride $(NSCl)_3$

1

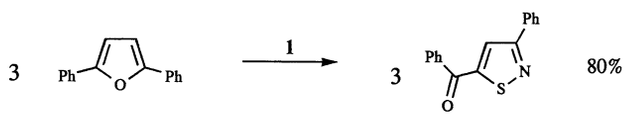


Scheme 1

In any given reaction the question arises as to whether the monomer and/or the trimer is the reacting species, and we hoped to gain some insight into this by studying possible Diels–Alder reactions between conjugated dienes and trithiazyl trichloride. Little is known about this, although [4 + 2] cycloadditions are possibly involved in the reactions with hexafluorobutadiene[5] and hexachlorocyclopentadiene.[6]

Reactions with furans

We chose 2,5-diphenylfuran as our first enophile. In boiling tetrachloromethane for four hours the trimer reacted very cleanly with the furan to give a stable dehydrochlorinated 1:1 adduct, $C_{16}H_{11}NOS$, in high yield (80%). This contained a conjugated carbonyl group (IR), probably part of a benzoyl group (MS), suggesting that the furan ring had undergone cleavage of an O–C bond, and an S–N unit had become incorporated. The product proved to be 5-benzoyl-3-phenylisothiazole **2**, in agreement with all the spectral data.



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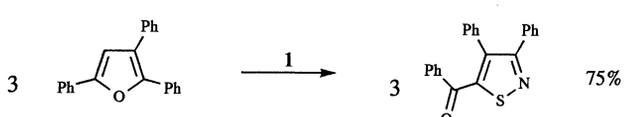


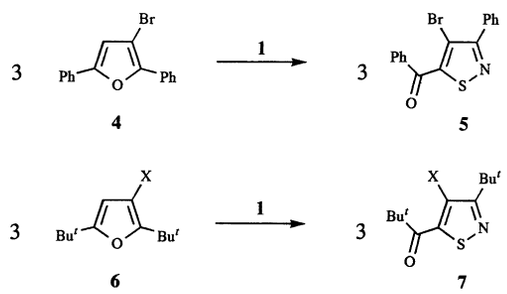
3

The same reaction was observed with 2,3,5-triphenylfuran which gave 5-benzoyl-3,4-diphenylisothiazole **3** in 75% yield. No isomers of these products were detected and so incorporation of the S–N unit is regiospecific.

The yields are based on the conversion of *three* molecules of the furan by one of the trimeric reagent **1**. This type of ring opening of furans is very rare; Huisgen recently reported the (possibly related) opening of 2-methoxyfuran and 2-*p*-tolyloxyfuran upon reaction with 2,3-bis(trifluoromethyl)fumaronitrile with formation of a carboxylic ester carbonyl group from the ring oxygen atom.[7]

The furan–trithiazyl trichloride reaction also provided a new and attractive (one-step) route to the isothiazoles **2** and **3**. Since there are still only a relatively limited number of good syntheses of this important ring system, we decided to explore the scope of this reaction. The only reported formation of isothiazoles by incorporation of the S–N unit are with allylic compounds: cholesteryl acetate and the trimer **1** gave a low yield (11%) of a fused isothiazole[4] and methacrylonitrile and the trimer in the presence of excess of sulfuryl chloride, which behaves as an equivalent of '$NSCl_3$', gave 5-cyanoisothiazole (78%).[8]

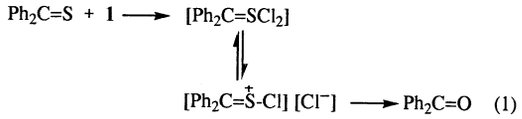
Treating 2,5-bis(4-methylphenyl)furan with trimer **1** in boiling tetrachloromethane for four hours gave the analogous 5-(4-methylbenzoyl)-3-(4-methylphenyl)isothiazole in 53%. An α-unsubstituted furan was chlorinated in this position by the trimer: 2,4-diphenylfuran gave 2-chloro-3,5-diphenylfuran (46%) as the major product, and 5-benzoyl-4-phenylisothiazole was not observed. Fully substituted furans such as 3,4-dibromo-2,5-diphenylfuran and 3-bromo-2,4,5-triphenylfuran did not react with **1**; clearly a ring hydrogen, for subsequent loss as hydrogen chloride, is a requirement for the reaction. 3-Bromo-2,5-diphenylfuran **4**, however, gave 5-benzoyl-4-bromo-3-phenylisothiazole **5** in excellent yield (85%).



The reactions of furan and 2,5-dimethylfuran with **1** were complex, even under milder conditions. With furan, various solvents (CCl_4, THF, PhMe and Et_2O) and neat furan were used at a number of temperatures from reflux down to −20 °C, but each led to a complex mixture. With 2,5-dimethylfuran it was suspected that the active hydrogens on the methyl groups were responsible for the complications and hence we turned to 2,5-di-*tert*-butylfuran. This reacted with trimer in boiling tetrachloromethane to give 3-*tert*-butyl-5-pivaloylisothiazole **7** (X = H) as the only isothiazole observed, and again the reaction was regiospecific. However the yield (40%) was disappointing; this may have resulted from the steric requirement of the *tert*-butyl groups and more forcing conditions were employed. The yield improved to 50% in boiling dioxane and 55% in boiling toluene. The 3-halogeno derivatives **6** (X = Br and Cl) gave the 3-*tert*-butyl-4-halogeno-5-pivaloylisothiazoles **7** (X = Br and Cl) in boiling toluene (50–55%), and again the 3,4-dibromo derivative gave no reaction with the trimer.

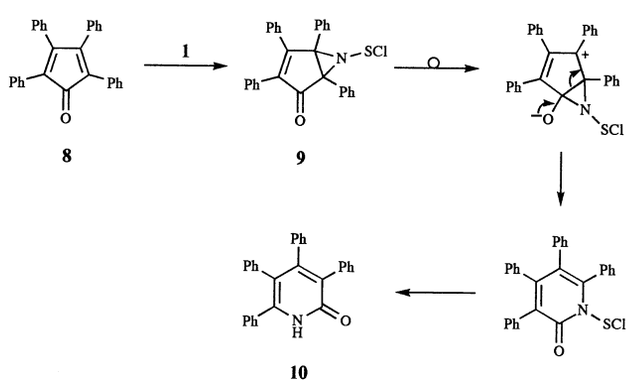
Reactions with thiophenes and tetraphenylcyclopentadienone

2,5-Diphenylthiophene was treated with the trimer **1** exactly as for the corresponding furan, in the expectation that the analogous thiobenzoylisothiazole **2** (S for O) would be formed; however the product proved to be the benzoylisothiazole **2** identical with that from 2,5-diphenylfuran. The thiophene was less reactive towards the trimer than the furan, in keeping with its greater aromaticity, and the best yield of **2** from the thiophene was only 25%, compared with 85% from the furan. We propose that the thiobenzoyl derivative **2** (S for O) is the initial product but under the reaction and work-up conditions this is converted into the ketone **2**. To test this, thiobenzophenone was prepared from benzophenone and phosphorus pentasulfide in refluxing carbon disulfide. On addition of the trimer to a solution of thiobenzophenone, the intense blue colour of the thioketone was immediately discharged to yield benzophenone which was isolated in 85% yield as the sole organic product after the standard chromatographic work-up. The trimer is possibly acting as a chlorinating agent to give an intermediate which is hydrolysed on silica gel [eqn. (1)]. It was shown in a similar



series of experiments that the trimer did not oxidise the more stable thioamide function in thiobenzamide, 1,1′-thiocarbonyldiimide, 2-mercaptobenzoxazole and 2-mercaptobenzothiazole.

Since thiophene 1,1-dioxides normally undergo Diels–Alder reactions, with loss of sulfur dioxide, much more readily than the parent thiophenes, 2,5-diphenylthiophene 1,1-dioxide, benzothiophene 1,1-dioxide, and 2,3-dibromobenzothiophene 1,1-dioxide were treated with the trimer in boiling tetrachloromethane, but no reaction was observed with any of these compounds. This suggests that they are too electron-deficient to undergo cycloaddition to the monomer or trimer or, alternatively, that the monomer/trimer reactions are not cycloadditions at all (see below). Finally a compound that is known to be a highly reactive Diels–Alder diene, tetraphenylcyclopentadienone (tetracyclone) **8**, was treated with the reagent **1** in boiling tetrachloromethane. It reacted very rapidly to give 3,4,5,6-tetraphenyl-2(1*H*)-pyridone **10** (56%) after crystallisation from ethanol; the same product was obtained in slightly lower yield (45%) when the reaction was run at room temperature. This reaction is reminiscent of that between tetracyclone **8** and hydrazoic acid to give the same pyridone **10**.[9] A possible mechanism, with the monomer adding as a nitrene, is shown in

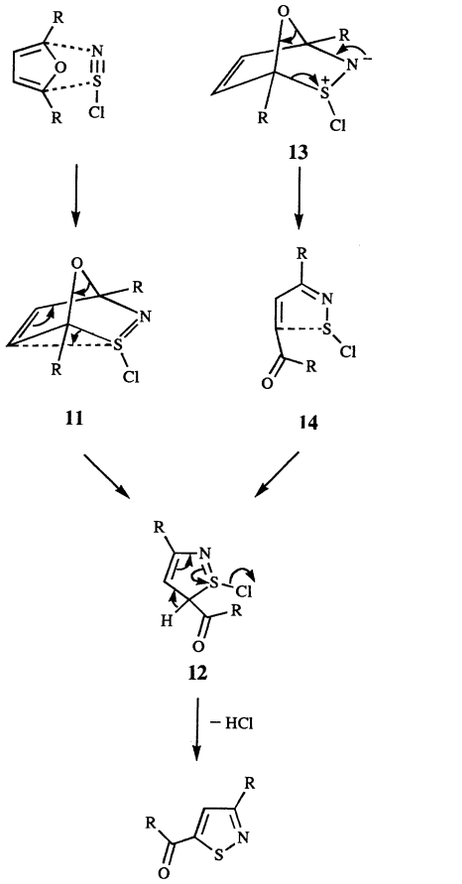


Scheme 2

Scheme 2; the rearrangement of the aziridine **9** so formed, and the N–S cleavage on work-up, could be catalysed by traces of hydrogen chloride generated from the moisture-sensitive reagent **1**. It is also possible that the monomer (or trimer) could undergo conjugate addition as a nitrogen nucleophile to the reactive Michael acceptor **8**, followed by collapse to aziridine **9** (or a related species).

Mechanism of the furan–trimer reactions

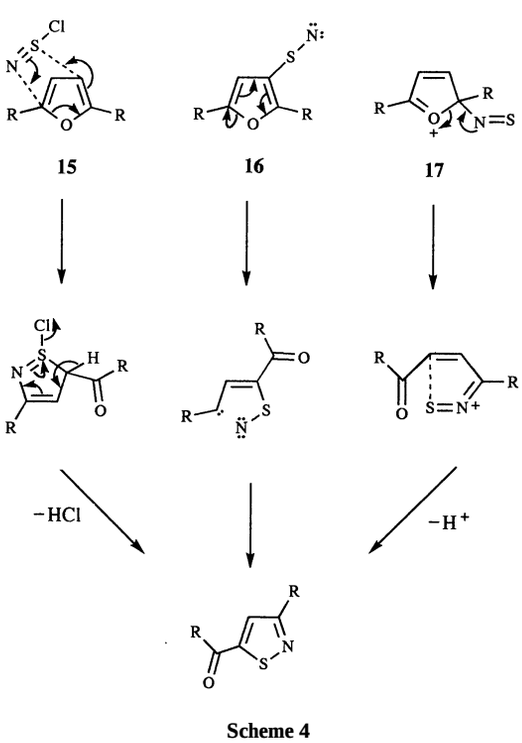
At the temperatures of these reactions the trimer **1** is substantially dissociated into the monomer and we assume that this highly reactive species is primarily responsible for the subsequent S–N transferring process, which is in keeping with the observed stoichiometry. Our original hypothesis was that thiazyl chloride would undergo cycloaddition to give the adduct **11** which would rearrange to **12** as shown (Scheme 3) and aromatise with loss of hydrogen chloride to give the isothiazole **2** isolated. The regiochemistry is controlled by which bridging C–O bond migrates and this is expected to be driven in the direction shown (arrows in **11**) by the strong polarisation ($S^+–N^-$) of the sulfur–nitrogen double bond. In the extreme, this polarisation could induce the cycloadduct **11** to open as



Scheme 3

shown in **13** to give the acyclic intermediate **14**, which could collapse to **12** or cyclise directly to the isothiazole.

Conversion of the furan into the isothiazole can also be represented formally as the cycloaddition of thiazyl chloride across the 2- and 4-positions of the furan ring **15**, with accompanying rearrangement, as shown in Scheme 4. The same overall transformation could be achieved by electrophilic attack on the furan by monomer (≡ NS^+Cl^-), through sulfur at the β-position **16** or through nitrogen at the α-position **17** (Scheme 4). The opposite modes of cycloaddition or of substitution would yield regioisomers which we have not observed with any of the furans studied. It is notable that the four 2,3,5-trisubstituted furans investigated (2,3,5-triphenyl, 3-bromo-2,5-diphenyl, 3-bromo-2,5-di-*tert*-butyl and 2,5-di-*tert*-butyl-3-chloro) each gave only one isothiazole product, cleanly and in good to very good yield. This would appear to argue against a mechanism initiated by attack at the (different) α-positions, and thus the Diels–Alder or β-substitution mechanisms are considered more likely and we are now trying to distinguish between them.



Scheme 4

Experimental

General details

Light petroleum refers to the fraction boiling between 60 and 80 °C which was distilled before use. Benzene, toluene, xylene and diethyl ether were dried over sodium wire for several days. Tetrahydrofuran was purified by distillation from potassium metal under nitrogen. Dichloromethane (DCM) and tetrachloromethane were dried by distillation from phosphorus pentaoxide and stored over 4 Å molecular sieves. Chloroform was washed with water, dried over sodium sulfate, distilled from phosphorus pentaoxide and stored over 4 Å molecular sieves. Pyridine was dried and distilled over potassium hydroxide.

Infra-red spectra were recorded on a Perkin-Elmer 1710FT spectrometer with internal calibration. ^{1}H HMR spectra were recorded on a JEOL GSX270 spectrometer at 270 MHz, a Bruker WM250 at 250 MHz, a Bruker AMX-400 at 400 MHz or a Bruker AM-500 at 500 MHz and ^{13}C spectra on the same machines at 69, 62.9, 100 and 125 MHz respectively. Chemical shifts are given in ppm, and are referenced to the residual peak of the solvent or to tetramethylsilane. Low resolution mass spectra and accurate mass measurements were recorded on a VG Micromass 7070B or VG Autospec instrument using electron impact ionisation unless stated otherwise.

Column chromatography was performed on either Merck Kieselgel 60H (70–230 mesh) or Crossfield 60H (60–230 mesh) silica. Samples were applied as a saturated solution in a suitable solvent or pre-adsorbed onto silica. TLC analysis was carried out on Merck Kieselgel GF_{254} aluminium-backed plates.

Trithiazyl trichloride 1 [10]

A mixture of disulfur dichloride (200 ml), ammonium chloride (200 g) and sulfur (50 g) was refluxed gently overnight. The air condenser bearing the dark brown crystals of $S_3N_2Cl_2$ which sublimed out of the reaction mixture was transferred to a predried flask and chlorine gas passed through the system. The S_2Cl_2 formed was removed under reduced pressure to leave trithiazyl trichloride as a bright yellow solid. The chlorination and removal of S_2Cl_2 was repeated until no more discolouration occurred on chlorination. The bright yellow trithiazyl trichloride was used without further purification. The residue from the formation of $S_3N_2Cl_2$ was destroyed by mixing thoroughly with solid sodium hydrogen carbonate.

5-Benzoyl-3-phenylisothiazole 2

Method (1). To a stirred solution of 2,5-diphenylfuran (550 mg, 2.5 mmol) in tetrachloromethane (10 ml), trithiazyl trichloride **1** (122 mg, 0.5 mmol) in tetrachloromethane (5 ml) was added dropwise. No significant temperature change was observed, but the solution turned green. The mixture was stirred at ambient temperature for 0.5 h and then heated at reflux for 2.5 h. The solvent was evaporated and the residue was separated by flash chromatography on silica gel. Elution with dichloromethane (40%) in light petroleum gave a minor product which was tentatively assigned as 5-benzoyl-4-chloro-3-

phenylisothiazole, *m/z* 301 (M^+, isotope, 7%), 299 (M^+, 19) in agreement with isotope cluster abundance calculations for $C_{16}H_{10}ClNOS$. Elution with dichloromethane (60%) in light petroleum gave 5-*benzoyl*-3-*phenylisothiazole* **2** as a clear oil (283 mg, 71% based on **1**) (Found: M^+, 265.0561. $C_{16}H_{11}NOS$ requires *M*, 265.0561); ν_{max}(neat)/cm^{-1} 3280 (Ar–H), 3062 (Ar–H), 2925, 2854, 1651 (C=O), 1598 (C=C), 1579, 1521, 1498, 1448, 1387, 1305, 1273, 1214, 1180, 1117, 1078, 1028, 975, 936, 910, 844, 793, 769; δ_H(270 MHz, $CDCl_3$) 7.42–7.60 (5H, m, ArH), 7.65–7.72 (1H, m, ArH), 7.96–8.02 (4H, m, ArH), 8.04 (1H, s, 4-H); δ_C(69 MHz, $CDCl_3$) 124.85 (CH), 126.95 (CH), 128.90 (CH), 128.98 (CH), 129.33 (CH), 139.72 (CH), 133.67, 134.11 (CH), 137.17, 164.94, 167.99, 186.34; *m/z* 266 (M^+ + 1, 17%), 265 (M^+, 91), 188 (M^+ − Ph, 25), 105 ($PhCO^+$, 100), 77 (Ph^+, 60).

Method (2). To a stirred solution of 2,5-diphenylfuran (190 mg, 0.84 mmol) in tetrachloromethane (10 ml) was added a solution of trithiazyl trichloride (68 mg, 0.28 mmol) in tetrachloromethane (5 ml). The reaction mixture was heated at reflux for 2.5 h, cooled and evaporated. The residue was separated on silica gel by chromatography. Elution with dichloromethane (40%) in light petroleum gave 5-benzoyl-3-phenylisothiazole, identical with the above product, as a clear oil (179 mg, 81%).

5-Benzoyl-3,4-diphenylisothiazole 3

To a mixture of benzil (15.8 g) and acetophenone (10.5 g), a solution of potassium hydroxide (3 g) in ethanol (54 ml) and water (4.5 ml) was added dropwise. The mixture was warmed and when the benzil was dissolved, the flask was allowed to stand for 2 days in the cold room (4 °C). The crystalline precipitate was collected and washed with a small amount of ethanol to give 1,2,4-triphenylbut-2-ene-1,4-dione (26 g). The crude product was heated at reflux with triethyl phosphite (17 ml) in triethylene glycol dimethyl ether (210 ml) for 3 h. The solvent was distilled at normal pressure and the residue was extracted with hexane; after cooling the crystals were collected and recrystallised from hexane to give 2,3,5-triphenylfuran as colourless crystals (15 g, 61%), mp 98–100 °C (lit.,[11] 93–94 °C); ν_{max}(Nujol)/cm^{-1} 1594, 1488, 1145, 1073, 1055, 1027, 953, 934, 904, 806, 756, 693, 662; δ_H(270 MHz, $CDCl_3$) 7.25–7.50 (12H, m, ArH), 7.60–7.67 (2H, m, ArH), 7.75–7.82 (2H, m, ArH).

To a solution of 2,3,5-triphenylfuran (592 mg, 2 mmol) in tetrachloromethane (1 ml) was added a solution of trithiazyl trichloride **1** (122 mg, 0.5 mmol) in tetrachloromethane (4 ml) with stirring at room temperature under nitrogen. During the addition no significant temperature change was observed, but the mixture turned green. The mixture was heated at reflux for 20 h. The resulting red solution was evaporated and the residue was separated by chromatography on silica gel. Elution with dichloromethane (60%) in light petroleum gave 5-*benzoyl*-3,4-*diphenylisothiazole* **3** as colourless needles (385 mg, 75%), mp 103.5–104.5 °C (Found: C, 77.7; H, 4.15; N, 4.2. $C_{22}H_{15}NOS$ requires C, 77.4; H, 4.4; N, 4.1%); ν_{max}(Nujol)/cm^{-1} 1675 (CO), 1633, 1598, 1580, 1515, 1392, 1349, 1310, 1269, 1224, 1182, 1097, 1075, 1029, 956, 935, 855, 781, 757, 729, 707; δ_H(270 MHz, $CDCl_3$) 7.04–7.17 (5H, m), 7.26–7.34 (5H, m), 7.38–7.50 (3H, m), 7.70–7.75 (2H, m); δ_C(69 MHz, $CDCl_3$) 128.04, 128.17, 128.29, 128.34, 128.87, 128.99, 129.77, 130.07, 132.87, 133.69, 134.77, 136.47, 138.60, 160.98, 166.92, 188.87; *m/z* 341 (M^+, 100%), 264 (M^+ − Ph, 12), 236 (M^+ − PhCO, 22), 105 ($PhCO^+$, 76), 77 (Ph^+, 74).

5-(4-Methylbenzoyl)-3-(4-methylphenyl)isothiazole

To a stirred solution of 2,5-bis(4-methylphenyl)furan[12] (266 mg, 1.06 mmol) in tetrachloromethane (2 ml), trithiazyl trichloride (84 mg, 0.34 mmol) in tetrachloromethane (5 ml) was added dropwise. The solution turned green. The mixture was heated at reflux for 4 h under nitrogen. The solvent was evaporated and the residue was separated by flash chromatography on silica gel. Elution with dichloromethane (40%) in light petroleum gave a minor product which was tentatively assigned the structure 5-(4-methylbenzoyl)-4-chloro-3-(4-methylphenyl)isothiazole (18 mg, 5%), *m/z* 327 (M^+, 18%), 293 (M^+ − Cl + H, 15), 119 ($CH_3C_6H_4CO^+$, 100). Elution with dichloromethane (50%) in light petroleum gave the *title compound* (163 mg, 53%), mp 100–101.5 °C (Found: C, 73.7; H, 5.1; N, 4.7. $C_{18}H_{15}NOS$ requires C, 73.7; H, 5.15; N, 4.8%); ν_{max}(Nujol)/cm^{-1} 1648 (C=O), 1603, 1501, 1418, 1405, 1311, 1283, 1263, 1211, 1203, 1179, 1111, 1069, 1042, 1016, 968, 953, 934; δ_H(270 MHz, $CDCl_3$) 2.35 (3H, s, CH_3), 2.45 (3H, s, CH_3), 7.27–7.36 (4H, m, ArH), 7.83–7.92 (4H, m, ArH), 7.95 (1H, s, 4-H); *m/z* 293 (M^+, 79%), 202 (M^+ − C_7H_7, 6), 174 (M^+ − $CH_3C_6H_4CO$, 4) 119 ($CH_3C_6H_4CO^+$, 100), 91 ($C_7H_7^+$, 39).

2-Chloro-3,5-diphenylfuran

To a stirred solution of 2,4-diphenylfuran[13] (210 mg, 0.95 mmol) in tetrachloromethane (10 ml) was added trithiazyl trichloride (72 mg, 0.3 mmol) in tetrachloromethane (5 ml). The reaction mixture was heated at reflux for 2.5 h. The solvent was evaporated and the residue was separated on silica gel by chromatography. Elution with dichloromethane (50%) in light petroleum gave 2-chloro-3,5-diphenylfuran as a pale green solid (110 mg, 46%), mp 253–254 °C; ν_{max}(Nujol)/cn^{-1} 3056, 1592, 1492, 1449, 1360, 1124, 1100, 1055, 1027, 966, 932, 908, 808, 755, 709, 689, 669; δ_H(270 MHz, $CDCl_3$) 6.88 (1H, s, 4-H), 7.26–7.46 (6H, m, ArH), 7.65 (2H, dd, ArH), 7.76 (2H, dd, ArH); *m/z* 256 (M^+, isotope, 12%), 254 (M^+, 38), 220 (M^+ − Cl + H, 87), 191 (M^+ − COCl, 100), 165 (13), 149 (12).

3,4-Dibromo-2,5-diphenylfuran

To a solution of 2,5-diphenylfuran (2.2 g, 10 mmol) in tetrachloromethane (25 ml) at room temperature was added *N*-bromosuccinimide (NBS) (2.2 equiv.). The mixture was stirred at room temperature until no starting material remained (TLC). The mixture was filtered through a pad of silica and the solvent removed under reduced pressure. The *title compound* was obtained as white needles, mp 89–91 °C; δ_H(270 MHz, $CDCl_3$) 8.18 (4H, m), 7.54 (6H, m); δ_C(69 MHz, $CDCl_3$) 147.9 (quat. C), 128.9 (C3 + C4 of furan ring), 128.4 (*p*- + *o*-C of Ph), 125.4 (*m*-C of Ph), 102.4 (quat. C) (Found: M^+ 377.9090. $C_{16}H_{10}Br_2O$ requires *M* 377.9078); *m/z* 380 [$(M + 2)^+$, 36%], 378 (M^+, 70), 376 [$(M - 2)^+$, 37], 105 ($PhCO^+$, 99), 77 (Ph^+, 100).

3-Bromo-2,4,5-triphenylfuran

To a mixture of 3,4-dibromo-2,5-diphenylfuran (440 mg, 1.17 mmol), phenylboronic acid (314 mg, 2.2 equiv.), benzene (2.5 ml), ethanol (0.8 ml, 20 equiv.) and 2 M aqueous sodium carbonate (2.6 ml, 4.4 equiv.) was added tetrakis(triphenylphosphine)palladium(0) (68 mg, 5 mol%). The mixture was heated at reflux until no starting material could be detected by TLC (24 h). The reaction mixture was poured into water, extracted with DCM and dried ($MgSO_4$). The solvent was removed under pressure and the product purified by column chromatography (eluent DCM–light petroleum). The title compound was isolated as a white solid (374 mg, 85%), mp 128–129 °C (lit.,[14] 129 °C); *m/z* 376 [$(M + 2)^+$, 75%], 374 (M^+, 77), 189 (46), 105 ($PhCO^+$, 98), 77 (Ph^+, 100).

5-Benzoyl-4-bromo-3-phenylisothiazole 5

To a solution of 2,5-diphenylfuran (2.2 g, 10 mmol) in tetrachloromethane (25 ml) at room temperature was added NBS (1 equiv.). The mixture was stirred at room temperature until no starting material remained (TLC). The mixture was filtered through a pad of silica and the solvent removed under reduced pressure to give 3-bromo-2,5-diphenylfuran **4** as an off-white solid, mp 65–66 °C (lit.,[15] 65–66 °C).

3-Bromo-2,5-diphenylfuran **4** (344 mg, 1 mmol) was dissolved in toluene (10 ml) and the mixture heated to reflux. The solution was allowed to cool slightly, the trimer **1** (80 mg,

0.33 equiv.) was added and the mixture was refluxed overnight. The solvent was removed under reduced pressure and the residue purified by column chromatography on silica gel (eluent DCM–light petroleum). The title compound **5** was isolated as a yellow oil (167 mg, 55%), identical with a sample prepared by bromination of 5-benzoyl-3-phenylisothiazole **2** with NBS as described for 2,5-diphenylfuran; *m/z* 346 [$(M + 2)^+$, 1.5%], 344 (M^+, 1.5), 264 [$(M - Br)^+$, 15], 105 ($PhCO^+$, 100), 77 (Ph^+, 59).

3-*tert*-Butyl-5-pivaloylisothiazole 7 (X = H)

2,5-Di-*tert*-butylfuran[16] (180 mg, 1 mmol) was dissolved in tetrachloromethane and the mixture heated to reflux. The solution was allowed to cool slightly, the trimer **1** (80 mg, 0.33 equiv.) was added and the mixture was refluxed overnight. The solvent was removed under reduced pressure and the residue purified by column chromatography on silica gel (eluent DCM–light petroleum). The *title compound* **7** (X = H) was isolated as a colourless oil, which crystallised on standing (40%), mp 29–31 °C (Found: C, 64.0; H, 8.4; N, 6.1. $C_{12}H_{19}NOS$ requires C, 64.0; H, 8.5; N, 6.2%); ν_{max}(neat)/cm^{-1} 1682 (C=O); δ_H(270 MHz, $CDCl_3$) 7.61 (1H, s, ring H), 1.37 (9H, s, Bu^t), 1.35 (9H, s, Bu^t); δ_C(125 MHz, $CDCl_3$) 198 (carbonyl C), 180 (C5 of het. ring), 162 (C3 of het. ring), 124 (C4 of het. ring), 44.2 (quat. C of pivaloyl), 36.5 (quat. C of *tert*-butyl), 30.0 (Me of pivaloyl), 27.2 (Me of *tert*-butyl); *m/z* 225 (M^+, 21%), 210 (16), 168 [$(M - Bu^t)^+$, 62], 141 [$(M - Bu^tCN)^+$, 34], 57 (Bu^{t+}, 100).

3-Bromo-2,5-di-*tert*-butylfuran 6 (X = Br)

2,5-Di-*tert*-butylfuran (1.8 g, 10 mmol) was dissolved in tetrachloromethane (20 ml) and NBS (1 equiv.) added. The mixture was stirred at room temperature for 2 days, filtered through a pad of silica and the title compound was isolated as a yellow oil; δ_H(270 MHz, $CDCl_3$) 5.95 (1H, s, ring H), 1.45 (9H, s, Bu^t), 1.30 (9H, s, Bu^t); *m/z* 260 [$(M + 2)^+$, 12%], 258 (M^+, 13), 243 [$(M - Me)^+$, 95], 121 [$(M - Bu^t - HBr)^+$, 45], 57 (Bu^{t+}, 28).

4-Bromo-3-*tert*-butyl-5-pivaloylisothiazole 7 (X = Br)

3-Bromo-2,5-di-*tert*-butylfuran **6** (X = Br) (258 mg, 1 mmol) was dissolved in toluene (10 ml) and the mixture heated to reflux. The solution was allowed to cool slightly, the trimer **1** (80 mg, 0.33 equiv.) was added and the mixture was refluxed overnight. The solvent was removed under reduced pressure and the residue purified by column chromatography on silica gel (eluent DCM–light petroleum). The *title compound* was isolated as a yellow oil (167 mg, 55%), identical with a sample prepared by bromination of 3-*tert*-butyl-5-pivaloylisothiazole with NBS as described for 2,5-diphenylfuran above; δ_H(270 MHz, $CDCl_3$) 1.36 (9H, s, Bu^t), 1.35 (9H, s, Bu^t); δ_C(69 MHz, $CDCl_3$) 203 (carbonyl C), 174 (C5 of het. ring), 159 (C3 of het. ring), 107 (C4 of het. ring), 46 (quat. C of pivaloyl), 39 (quat. C of *tert*-butyl), 29 (Me of pivaloyl), 26 (Me of *tert*-butyl); *m/z* 305 [$(M + 2)^+$, 0.4%], 246 [$(M - Bu^t)^+$, 13.6], 57 (Bu^{t+}, 100).

2,5-Di-*tert*-butyl-3-chlorofuran 6 (X = Cl)

2,5-Di-*tert*-butylfuran (1.8 g, 10 mmol) was dissolved in tetrachloromethane (20 ml) and *N*-chlorosuccinimide (NCS) (1 equiv.) added. The mixture was stirred at room temperature for 2 days and then separated by filtration through a pad of silica. The title compound was isolated as a yellow oil (1.68 g, 65%); δ_H(270 MHz, $CDCl_3$) 7.51 (1H, s, het. ring H), 1.26 (18H, s, 2 × Bu^t); *m/z* 258 (M^+, 13%), 243 (95), 121 (45), 57 (Bu^{t+}, 28).

3-*tert*-Butyl-4-chloro-5-pivaloylisothiazole 7 (X = Cl)

2,5-Di-*tert*-butyl-3-chlorofuran (260 mg, 1 mmol) was dissolved in toluene (10 ml) and the mixture heated to reflux. The solution was allowed to cool slightly and the trimer **1** (80 mg, 0.33 equiv.) was added and the mixture was then refluxed overnight. The solvent was removed under reduced pressure and the residue purified by column chromatography on silica gel (eluent DCM–light petroleum). The title compound was isolated as a yellow oil (130 mg, 50%), identical with a sample prepared by chlorination of 3-*tert*-butyl-5-pivaloylisothiazole with NCS as described for 2,5-diphenylfuran above; δ_H(270 MHz, $CDCl_3$) 1.36 (9H, s, Bu^t), 1.33 (9H, s, Bu^t); δ_C(69 MHz, $CDCl_3$) 202 (carbonyl C), 173 (C5 of het. ring), 156 (C3 of het. ring), 107 (C4 of het. ring), 46 (quat. C of pivaloyl), 39 (quat. C of *tert*-butyl), 29 (Me of pivaloyl), 26 (Me of *tert*-butyl); *m/z* 261 [$(M + 2)^+$, 0.3%], 259 (M^+, 0.8) [$(M - Bu^t)^+$, 3.5], 57 (Bu^{t+}, 100).

3,4-Dibromo-2,5-di-*tert*-butylfuran

To a solution of 2,5-di-*tert*-butylfuran (1.8 g, 10 mmol) in tetrachloromethane (20 ml) was added NBS (2.2 equiv.). The mixture was stirred at room temperature for 1 week and the mixture filtered through a pad of silica. The title compound was isolated as a yellow oil (2.81 g, 83%); δ_H(270 MHz, $CDCl_3$) 1.36 (s, 2 × Bu^t); *m/z* 388 (M^+, 16%), 323 [$(M - Me)^+$, 91], 199 [$(M - Br - Bu^t)^+$, 29], 57 (Bu^{t+}, 100).

Reaction of 2,5-diphenylthiophene with trithiazyl trichloride

2,5-Diphenylthiophene[17] had mp 151–152 °C (lit.,[17] 149–150 °C); δ_H(60 MHz, $CDCl_3$) 6.7 (2H, s, thiophene ring protons), 7.2–7.5 (6H, m, PhH), 7.6–8.0 (4H, m, PhH). To a stirred solution of 2,5-diphenylthiophene (210 mg, 0.88 mmol) in tetrachloromethane (10 ml) under nitrogen, trithiazyl trichloride (72 mg, 0.3 mmol) in tetrachloromethane (4 ml) was added dropwise. The reaction mixture was heated at reflux for 2.5 h. The solvent was evaporated to give a brown oil which was purified by chromatography on silica gel. Elution with dichloromethane (60%) in light petroleum gave an orange oil (90 mg) which slowly became darker. It was rechromatographed to give 5-benzoyl-3-phenylisothiazole **2** (40 mg, 17%), identical with that described earlier. Yields of up to 25% were obtained in repeat experiments.

Thiobenzophenone

A suspension of benzophenone (18.2 g), phosphorus pentasulfide (6.7 g) and triethylamine (10 ml) in carbon disulfide (45 ml) was refluxed gently for 1 h under nitrogen. The mixture was filtered, and the CS_2 removed under reduced pressure. The thiobenzophene was sublimed from the deep blue residue at reduced pressure (0.5 mmHg) to give bright blue crystals mp 46–47 °C (lit.,[18] 50–51 °C).

Reaction of thiobenzophenone with the trimer

Thiobenzophenone (396 mg, 2 mmol) was dissolved in tetrachloromethane (15 ml) and the mixture heated to reflux. The solution was allowed to cool slightly and the trimer **1** (500 mg, 1 equiv.) added; the bright blue colour of the solution disappeared immediately. The mixture was refluxed for a further 1 h, the solvent removed under reduced pressure and the residue purified by column chromatography. Benzophenone (310 mg, 85%) was isolated as the sole organic product, identical with an authentic sample.

3,4,5,6-Tetraphenylpyridin-2(1*H*)-one 10

Method (1). Tetraphenylcyclopentadienone **8** (384 mg, 1 mmol) was dissolved in tetrachloromethane (15 ml) and the mixture heated to reflux. The solution was allowed to cool slightly and the trimer **1** (245 mg, 1 equiv.) added. The deep purple colour of the solution disappeared immediately on addition of the trimer. The mixture was then refluxed overnight. The precipitate was filtered off and recrystallised from ethanol. The title compound was isolated as white needles (224 mg, 56%), identical with an authentic sample, mp 271–273 °C (lit.,[9] 272–273 °C); *m/z* 399 (M^+, 75%), 388 [$(M - 1)^+$, 100].

Method (2). Tetraphenylcyclopentadienone (384 mg, 1 mmol) was dissolved in tetrachloromethane (15 ml) and the trimer (245 mg, 1 equiv.) added at room temperature. The deep purple colour of the solution disappeared rapidly. The mixture was then

stirred at room temperature overnight. The precipitate was filtered off and recrystallised from ethanol. The title compound (180 mg, 45%), was identical with that described above.

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