Reactions of Tetrasulfur Tetranitride with Alkyl Aryl Ketoximes: Synthesis of 3-Aryl- and 3-Alkyl-4-aryl-1,2,5-thiadiazoles

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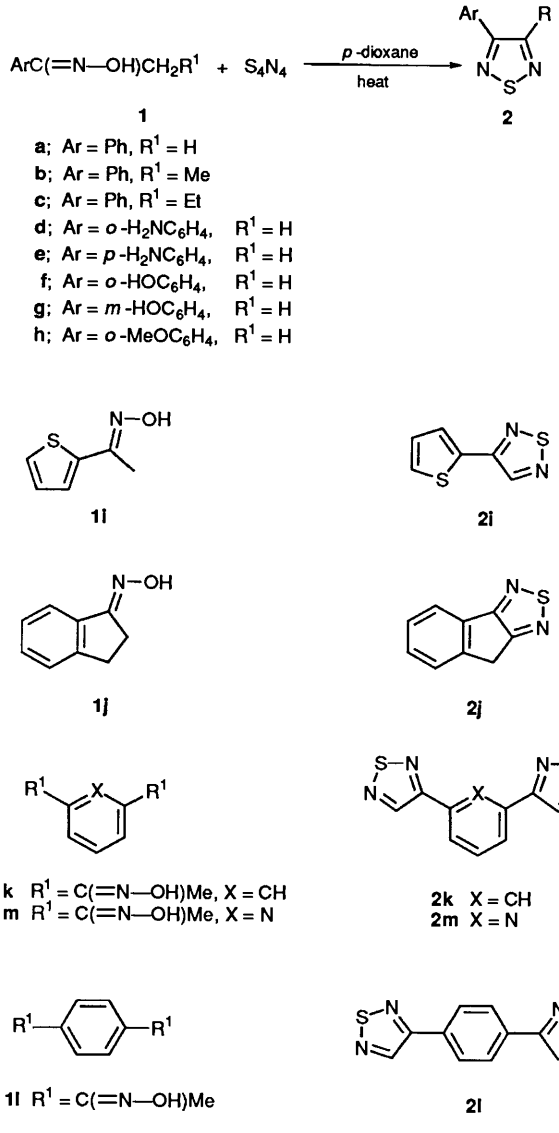
Tetrasulfur tetranitride (S_4N_4) was treated with various alkyl aryl ketoximes having two hydrogens at the α-carbon atom to the oxime functionality in *p*-dioxane at reflux to give 3-substituted and 3,4-disubstituted 1,2,5-thiadiazoles in moderate yields. Reaction with isobutyrophenone oxime under the same conditions did not give the 1,2,5-thiadiazole derivative. On the other hand, the reaction with cyclohexanone oxime in *p*-dioxane and toluene afforded 4,5-dihydrobenzo[1,2-*c*:3,4-*c*']bis[1,2,5]-thiadiazole in 6 and 7% yield, respectively.

Much effort has been devoted to developing new synthetic utilities of tetrasulfur tetranitride (S_4N_4),[1] particularly focusing on one-step synthesis of sulfur- and nitrogen-containing organic compounds. Although numerous aromatic hydrocarbons and ketones were treated with S_4N_4, the major products were 3,4-disubstituted 1,2,5-thiadiazoles in most cases albeit with low yields and the mechanistic details of the formation of the products were seldom described. Recently we have studied the reactions of S_4N_4 with α-monohalogenomethyl aryl ketones and alkyl ketones without α-hydrogens in order to observe the effects of halogen as a leaving group.[2] Surprisingly, from the former were obtained 3,5-diaroyl-1,2,4-thiadiazoles and from the latter 3,5-diacyl-1,2,4-thiadiazole as a major product. No 1,2,5-thiadiazole derivatives were detected. Except for 3,5-dibenzoyl-1,2,4-thiadiazole,[3] all of the 3,5-diaroyl- and 3,5-diacyl-1,2,4-thiadiazoles prepared were new compounds. To our knowledge, this is the first general synthetic method for 3,5-diaroyl- and 3,5-diacyl-1,2,4-thiadiazoles.

In a continuation of our efforts to explore new synthetic methodologies using S_4N_4 and to gain insight into their mechanisms, we were aware of the fact that the reactions of S_4N_4 with only a limited number of ketoximes such as benzophenone oxime, fluorenone oxime, and benzil monoxime have been studied.[4] All of the oximes used have no α-hydrogens around the oxime functionality. On the other hand, cyclohexanone oxime, which is the only known example studied as a ketoxime having α-hydrogens, gave only large amounts of intractable tar under the same conditions.[4] No further study has been made on the reactions of the oximes with S_4N_4 up until now. We were interested in a study of the reactions of S_4N_4 with various ketoximes having α-hydrogens to ascertain the effects of the α-hydrogens of ketoximes. The results are described herein.



Results and Discussions

Heating of equimolar amounts of (*E*)-acetophenone oxime **1a**[5] and S_4N_4 in toluene at reflux until S_4N_4 had completely disappeared showed many spots with a long tail connected to the origin on TLC (silica gel; CCl_4) and black tarry material appeared increasingly with reaction time. From chromatography of the reaction mixture were isolated 3-phenyl-1,2,5-thiadiazole **2a** in 21% yield along with sulfur, small amounts of oily liquids, and black tarry material. No 1,2,4-thiadiazole derivative was detected. The reaction was repeated in *p*-dioxane under the same conditions to give compound **2a** in 35% yield. No 1,2,4-thiadiazole derivative was detected in this case either. Since *p*-dioxane was a better solvent than toluene with respect to the solubilities of ketoximes as well as giving a 'cleaner' reaction and a better yield of compound **2a**, the reactions of various ketoximes **1** with S_4N_4 were carried out in *p*-dioxane at reflux. The results are summarized in Table 1.

About 4 to 5 mmol of an oxime **1** and a slight molar excess of S_4N_4 were used for the reactions of oximes **1a**–**1j** until TLC no longer showed the spot corresponding to S_4N_4. However, about a two-fold molar excess of S_4N_4 was used in the reactions of oximes **1k**–**1m** because a significant amount of oxime remained

Table 1 Synthesis of 3-substituted and 3,4-disubstituted-1,2,5-thiadiazoles **2**

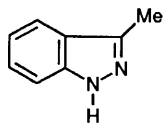
Compound		Reaction time (t/h)	Yield (%)[a]
2a	Ar = Ph, R^1 = H	48	35[b]
	Ar = Ph, R^1 = H	48	31[c]
2b	Ar = Ph, R^1 = Me	48	42
2c	Ar = Ph, R^1 = Et	48	36
2d	Ar = *o*-$H_2NC_6H_4$, R^1 = H	2.5	7[d]
2e	Ar = *p*-$H_2NC_6H_4$, R^1 = H	24	33
2f	Ar = *o*-HOC_6H_4, R^1 = H	48	20
2g	Ar = *m*-HOC_6H_4, R^1 = H	36	41
2h	Ar = *o*-$MeOC_6H_4$, R^1 = H	48	*e*
2i		36	44
2j		24	33
2k		60	26
2l		60	38
2m		72	48

[a] Isolated yields by column chromatography. [b] Yield obtained from (*E*)-isomer **1a**. [c] Yield obtained from (*Z*)-isomer **1a**. [d] 3-Methylindazole **3** was a major product (26%). [e] *o*-Methoxyacetophenone (3%) and unidentifiable compounds were obtained.

unchanged even when decomposition of S_4N_4 was complete.

Among the 1,2,5-thiadiazoles prepared, **2a**, **2b**, **2c**, **2i** and **2j** are known compounds. Compound **2a** was prepared by the reaction of S_4N_4 with ethylbenzene[6] or phenylacetylene[7] in toluene at reflux, and with acetophenone[8] without using any solvent at 85–95 °C. The yields of compound **2a** in the last two reactions were reported to be 16 and 35%, respectively. Since the (*E*)-isomer of **1a** [(*E*)-**1a**] gave a 35% yield of compound **2a**, the (*Z*)-isomer of oxime **1a** [(*Z*)-**1a**][5] was prepared and subjected to the same reaction conditions. The reaction of (*Z*)-**1a** gave compound **2a** in 31% yield, which is close to the yield from (*E*)-**1a** within experimental error. It has been reported that (*Z*)-**1a** isomerizes to (*E*)-**1a** quantitatively at 132 °C, and the ^{1}H NMR ($CDCl_3$) signal of the methyl group of (*Z*)-**1a** appeared at δ_H 2.20 and that of (*E*)-**1a** at δ_H 2.28.[5] We have confirmed the results by ^{1}H NMR spectroscopy (80 MHz; $CDCl_3$), by using an equimolar mixture of (*Z*)- and (*E*)-**1a**. We found that (*Z*)-**1a** isomerized to (*E*)-**1a** in refluxing *p*-dioxane even in 30 min, by which time the ^{1}H NMR spectrum showed only the presence of (*E*)-**1a**. Since it takes 48 h for the complete decomposition of S_4N_4 (Table 1, **2a**), it is conceivable that rapid isomerization of (*Z*)-**1a** to (*E*)-**1a**, followed by reaction with S_4N_4 can occur. Compound **2c** was prepared in 14% yield by heating a mixture of S_4N_4 and 1-amino-1-phenylbutane in xylene for 6 h at reflux.[9] Accordingly it would be better for compound **2c** to be prepared from oxime **1c** in view of the yield of product **2c** and the ready availability of the reactant. The reaction with *o*-aminoacetophenone oxime **1d** in *p*-dioxane at reflux showed spots corresponding to 3-methylindazole **3** [R_f 0.14 (CH_2Cl_2)] and to compound **2d** [R_f 0.55 (CH_2Cl_2)]. However, the spot of the latter gradually faded during 24 h, concomitant with the formation of lots of tarry material which caused the separation of the indazole **3** by column chromatography to be difficult. By allowing a shorter reaction time (2.5 h), compounds **2d** and **3** were isolated in 7 and 26% yield, respectively, as well as unchanged **1d** (5%) and S_4N_4 (30%).

The structure of compound **3** was identified based on the spectroscopic data and by comparison of its m.p. with that reported.[10] However, the mechanism of the formation of compound **3** is not known. On the other hand, the reaction of *p*-aminoacetophenone oxime **1e** afforded compound **2e** in 33% yield as an identifiable product in addition to sulfur. From the reaction of *o*-hydroxyacetophenone oxime **1f** was isolated



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compound **2f** in 20% yield together with sulfur and other inseparable mixtures. There are reports[8,11] in which compound **2f** could not be detected in the reaction of *o*-hydroxyacetophenone with S_4N_4. Reaction of *m*-hydroxyacetophenone oxime **1g** gave compound **2g** in 41% yield. It is interesting to know that equimolar amounts of 2,4-dimethyl-, 4-(*tert*-butyl)-2-methyl-, and 2,4-di(*tert*-butyl)phenols reacted with S_4N_4 in toluene at reflux for 6 h to give the 2,1,3-benzothiadiazoles.[12] No 2,1,3-benzothiadiazoles were detected in either of the reactions with substrates **1f** and **1g**. Reaction of *o*-methoxyacetophenone oxime **1h** did not give the corresponding 1,2,5-thiadiazole **2h** at all. Instead, *o*-methoxyacetophenone (3%) and an unknown compound whose structure has not been characterized were isolated. Reaction of (*E*)-2-acetylthiophene oxime **1i**[13] afforded compound **2i** in 44% yield, which was previously prepared in 10% yield by the reaction of 2-acetylthiophene with S_4N_4 at 85–95 °C without using a solvent.[8] Reaction of indan-1-one oxime **1j** afforded compound **2j** in 33% yield, which was previously prepared in 20% yield by the reaction of indan-2-one with S_4N_4 in toluene at reflux.[11] *m*-(**1k**) and *p*-Diacetylbenzene oximes (**1l**) were insoluble even in boiling toluene. Therefore, toluene was inappropriate as a solvent for the reactions of oximes **1k** and **1l**. Their reactions in *p*-dioxane proceeded slowly as shown in Table 1. The reaction of 2,6-diacetylpyridine **1m** proceeded more slowly but more cleanly than that of either oxime **1k** or **1l**, and the yield of compound **2m** was the highest of the reactions we have tried.

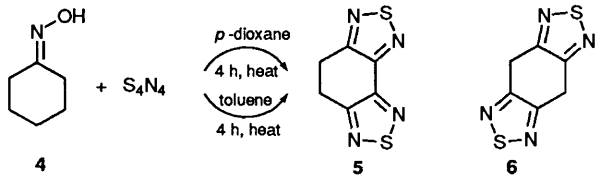
A substituent at an *ortho* position seems to reduce the yields of thiadiazoles **2** compared with those of the regioisomers as shown in the yields of compounds **2d** and **2e**, and **2f** and **2g**. The *ortho* effects might be rationalized in terms of either steric effects or the participation of the *ortho* substituent in another reaction, as shown clearly in the reaction of oxime **1d**: isolation of the indazole **3** as a main product. The fact that no 1,2,5-thiadiazole derivative was formed in the reaction of oxime **1h** can be explained in the same fashion. Although both the hydroxy and methoxy groups are electron-donating groups, both groups are known to participate differently in the reaction with S_4N_4. For example, the reactions of anisole and 1,2- and 1,3-dimethoxybenzene in toluene at 120 °C for 24 h afforded benzo[1,2-*c*:3,4-*c*':5,6-*c*'']tris[1,2,5]thiadiazole and benzo[1,2-*c*:3,4-*c*']bis[1,2,5]thiadiazoles in small yield,[14] respectively, whereas the reactions of equimolar amounts of 4-methyl or 4-(*tert*-butyl)-phenol in toluene at reflux for 6 h afforded 2,1,3-benzothiadiazoles.[12]

The reaction of isobutyrophenone oxime, which has only one α-hydrogen, under the same reaction conditions as for other ketoximes was so complicated that no identifiable product has been isolated.

Since the presence of at least two α-hydrogens of an alkyl aryl ketoxime **1** might be a necessary condition for the formation of 1,2,5-thiadiazoles **2**, the reaction of cyclohexanone oxime **4** with S_4N_4 was investigated under the same conditions as used for oximes **1**. From the reaction were isolated 4,5-dihydrobenzo-[1,2-*c*:3,4-*c*']bis[1,2,5]thiadiazole **5** in 6% yield along with sulfur and unidentifiable complex mixtures. The same reaction was carried out in toluene at reflux for 4 h and compound **5** was isolated in 7% yield. Besides, a liquid which showed one spot on TLC but two peaks (48:52, t_R 6.52 min:6.96 min) on HPLC (MeCN) was separated from the reaction mixture. Separation and characterization of the mixture has not been successful. The

structure of compound **5** was assigned based on spectroscopic and mass spectral data and elemental analysis. The ^{1}H NMR (80 MHz; $CDCl_3$) spectrum showed a singlet at δ_H 3.43, and the ^{13}C NMR (50.3 MHz; $CDCl_3$) spectrum showed three peaks, at δ_C 25.32, 151.25 and 161.48. The ^{13}C NMR data clearly ruled out the structure **6** from which two peaks of ^{13}C NMR were expected. On the other hand, the reaction of cyclopentanone oxime in either toluene or *p*-dioxane at reflux for 4 h afforded only the intractable tarry material, sulfur, and a small amount of unchanged S_4N_4.

Compound **5** is a new compound although its structure is similar to that of naphtho[1,2-*c*:3,4-*c*′]bis[1,2,5]thiadiazole as far as the bonding between two 1,2,5-thiadiazole rings in the molecule is concerned. The latter compound was prepared by the reaction of tetrahydronaphthalene with S_4N_4 *via* 4,5-dihydronaphtho[1,2-*c*][1,2,5]thiadiazole in two steps.[15] A free-radical mechanism was proposed for the formation of the compound because of the presence of benzylic hydrogens as well as other experimental evidence. However, compound **4** has no benzylic hydrogens. Recently, Mataka *et al.*[16] obtained naphtho[1,2-*c*:3,4-*c*′]bis[1,2,5]thiadiazole from the reaction of 1-naphthol with S_4N_4. The mechanism of formation of the compound was not described. Nonetheless the author suggested the involvement of two tautomers of 1-naphthol. However, it is uncertain at this moment whether the initial step in the reactions of the oximes with S_4N_4 involves the direct nucleophilic attack of the hydroxy group of the oximes on S_4N_4[4] or not. Further study is in progress.



4 **5** **6**

Experimental

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. IR spectra were obtained on a Perkin-Elmer Model 283 spectrometer as KBr pellets or thin films on KBr plate. ^{1}H NMR spectra were determined on either Bruker 80 MHz or EM360A 60 MHz spectrometers using tetramethylsilane as internal standard. ^{13}C NMR spectra were recorded on a Varian VXR-200S spectrometer operating at 50.3 MHz. HPLC was performed on a Waters Model 510 with refractometer using μBondapak C_{18} 10 μm column. Mass spectra were obtained by electron impact at 70 eV on a Varian MAT 711. Elemental analyses were determined by the Korea Basic Science Center. Column chromatography was performed on silica gel (Merck 230–400 mesh, ASTM).

Tetrasulfur tetranitride was prepared by the reaction of sulfur monochloride with ammonia gas at room temperature.[1] Oximes were prepared by the literature methods:[17] (*E*)-acetophenone oxime (*E*)-**1a**, m.p. 58–59 °C (lit.,[18a] 59.5–60.5 °C); (*Z*)-acetophenone oxime (*Z*)-**1a**, m.p. 79–80 °C (lit.,[5] 81–83 °C); propiophenone oxime **1b**, m.p. 52–53 °C (lit.,[18b] 53–54 °C); butyrophenone oxime **1c**, m.p. 49–50 °C (lit.,[18c] 50 °C); *o*-aminoacetophenone oxime **1d**, m.p. 110–111 °C (lit.,[18d] 111–112 °C); *p*-aminoacetophenone oxime **1e**, m.p. 146–147 °C (lit.,[18e] 147–148 °C); *o*-hydroxyacetophenone oxime **1f**, m.p. 114–116 °C (lit.,[18f] 117 °C); *o*-methoxyacetophenone oxime **1h**, m.p. 82–83 °C (lit.,[17] 83 °C); 2-acetylthiophene oxime **1i**, m.p. 111–112 °C (lit.,[10,19] 112–113 °C); (*E*)-indan-1-one oxime **1j**, m.p. 151–153 °C (lit.,[20] 153–154 °C); *m*-diacetylbenzene dioxime **1k**, m.p. 237–238 °C (lit.,[18g] 238–240 °C); *p*-diacetylbenzene dioxime **1l**, m.p. 239 °C (lit.,[18h] 240 °C); cyclohexanone oxime **4**, m.p. 88–89 °C (lit.,[18i] 89–91 °C); *m*-hydroxyacetophenone oxime **1g**, oily liquid (Found: C, 63.6; H, 6.3; N, 8.8. $C_8H_9NO_2$ requires C, 63.56; H, 6.00; N, 9.27%); ν_{max}(film)/cm^{-1} 3600–2500, 1586, 1494, 1448, 1372, 1312, 1218, 1166, 1100, 1082, 1010, 958, 876, 789, 751, 694 and 658; δ_H(60 MHz; $CDCl_3$) 2.24 (3 H, s, Me), 6.95–7.86 (5 H, m, Ph and OH) and 9.87 (1 H, s, NOH); 2,6-diacetylpyridine dioxime **1m**, m.p. 240–242 °C (from EtOH) (Found: C, 55.1; H, 5.9; N, 21.9. $C_9H_{11}N_3O_2$ requires C, 55.95; H, 5.74; N, 21.75%); δ_H[60 MHz; $(CD_3)_2SO$–$CDCl_3$ (3:1)] 2.31 (6 H, s, 2 × Me), 7.65–8.19 (3 H, m, ArH) and 11.37 (2 H, s, 2 × OH); ν_{max}(KBr)/cm^{-1} 3600–2500, 1570, 1453, 1364, 1345, 1254, 1168, 1131, 1117, 1094, 1020, 965, 839, 811, 752, 730 and 687.

General Procedure for the Reaction of Ketoximes with S_4N_4.—A mixture of a ketoxime (4–5 mmol) and a slight molar excess of S_4N_4 in *p*-dioxane (20 cm^3) was refluxed until S_4N_4 had disappeared completely. The progress of the reaction was monitored by TLC [R_f of S_4N_4 0.75 (benzene)]. The reaction mixture was cooled to room temperature, followed by filtration. After removal of the solvent under reduced pressure, the residue was chromatographed on silica gel. Elution with hexane gave sulfur, and then the 1,2,5-thiadiazole derivatives **2** were eluted by using a series of solvents (see below).

3-*Phenyl*-1,2,5-*thiadiazole* **2a**. (a) A mixture of (*E*)-acetophenone oxime (*E*)-**1a** (543 mg, 4.02 mmol) and S_4N_4 (817 mg, 4.43 mmol) in *p*-dioxane (20 cm^3) was refluxed for 48 h. The mixture was chromatographed on silica gel (2 × 12 cm). After removal of sulfur, elution with a mixture of hexane–benzene (3:1; 200 cm^3) gave the title compound **2a** (231 mg, 1.42 mmol, 35%), m.p. 42–43 °C (from Et_2O) (lit.,[8] 42–44 °C).

(b) A mixture of (*Z*)-acetophenone oxime (*Z*)-**1a** (551 mg, 4.08 mmol) and S_4N_4 (820 mg, 4.45 mmol) was treated as for the (*E*)-isomer. Chromatography gave the title compound **2a** (206 mg, 1.27 mmol, 31%).

3-*Methyl*-4-*phenyl*-1,2,5-*thiadiazole* **2b**. A mixture of propiophenone oxime **1b** (598 mg, 4.01 mmol) and S_4N_4 (813 mg, 4.41 mmol) in *p*-dioxane was refluxed for 48 h. Chromatography of the reaction mixture using a mixture of hexane–benzene (3:1) gave the title compound **2b** (298 mg, 1.69 mmol, 42%) as an oily liquid; δ_H(60 MHz; $CDCl_3$) 2.71 (3 H, s, Me) and 7.23–7.85 (5 H, m, Ph).

3-*Ethyl*-4-*phenyl*-1,2,5-*thiadiazole* **2c**. A mixture of butyrophenone oxime **1c** (664 mg, 4.07 mmol) and S_4N_4 (818 mg, 4.44 mmol) in *p*-dioxane was refluxed for 48 h. Chromatography as for compound **2a** using hexane gave a mixture of sulfur, **2c**, and other compounds, which were rechromatographed using hexane to give the title compound **2c** (283 mg, 1.46 mmol, 36%) as an oily liquid; δ_H(60 MHz; $CDCl_3$) 1.47 (3 H, t, Me), 3.11 (2 H, q, CH_2) and 7.23–7.95 (5 H, m, Ph).

3-(o-*Aminophenyl*)-1,2,5-*thiadiazole* **2d**. A mixture of *o*-aminoacetophenone oxime **1d** (634 mg, 4.22 mmol) and S_4N_4 (821 mg, 4.46 mmol) in *p*-dioxane was refluxed for 2.5 h. Chromatography of the reaction mixture using a mixture of hexane–benzene (1:1) gave unchanged S_4N_4 (250 mg, 1.36 mmol, 30%).

Elution next with benzene gave the *title compound* **2d** (55 mg, 0.31 mmol, 7%) as a sticky, oily liquid (Found: C, 54.2; H, 3.9; N, 23.8. $C_8H_7N_3S$ requires C, 54.22; H, 3.98; N, 23.71%); ν_{max}(film)/cm^{-1} 3452 and 3341 (NH_2), 1612, 1484, 1444, 928, 786, 755 and 741; δ_H(60 MHz; $CDCl_3$) 5.8 (2 H, br s, NH_2), 6.71–8.02 (4 H, m, Ph) and 9.13 (1 H, s, N=CH); *m*/*z* 177 (100%, M$^+$), 150 (33.7, M − HCN) and 118 (66.8, M − HCNS).

Elution next with methylene dichloride, followed by a mixture of hexane–ethyl acetate (3:2), gave starting material **1d** (35 mg, 0.23 mmol, 5% recovery) and a mixture, respectively. The latter was rechromatographed to give 3-methylindazole **3** (144 mg, 1.09 mmol, 26%), m.p. 110–111 °C (from hexane) (lit.,[10]

112–113 °C); ν_{max}(film)/cm^{-1} 3300 (NH), 1614, 1497, 1451, 1336, 1254, 1009, 987, 766 and 749; δ_H(60 MHz; $CDCl_3$) 2.62 (3 H, s, Me), 7.01–7.95 (4 H, m, Ph) and 11.01 (1 H, br s, NH); *m/z* 132 (100%, M$^+$), 131 (97.9), 104 (17.7), 78 (10.1) and 77 (15.4).

3-(p-*Aminophenyl*)-1,2,5-*thiadiazole* **2e**. A mixture of *p*-aminoacetophenone oxime **1e** (618 mg, 4.12 mmol) and S_4N_4 (819 mg, 4.44 mmol) in *p*-dioxane was refluxed for 24 h. Repeated chromatography using a mixture of hexane–ethyl acetate (3:1) gave an oily liquid (18 mg) and the *title compound* **2e** (238 mg, 1.34 mmol, 33%), m.p. 100.5–102 °C (from CCl_4) (Found: C, 54.15; H, 3.9; N, 23.7%); ν_{max}(KBr)/cm^{-1} 3361, 3300, 3200, 1600, 1529, 1476, 1352, 1286, 1221, 1183, 1151, 1097, 926, 881, 838, 783, 676 and 528; δ_H(80 MHz; $CDCl_3$) 3.91 (2 H, br s, NH_2), 6.74 (2 H, *J* 8.8 Hz, Ph), 7.79 (2 H, *J* 8.8 Hz, Ph) and 8.78 (1 H, s, N=CH); *m/z* 177 (100%, M$^+$), 150 (63.1, M − HCN) and 118 (90.0, M − HCNS).

3-(o-*Hydroxyphenyl*)-1,2,5-*thiadiazole* **2f**. A mixture of 2-hydroxyacetophenone oxime **1f** (611 mg, 4.04 mmol) and S_4N_4 (814 mg, 4.42 mmol) in *p*-dioxane was refluxed for 48 h. Chromatography of the reaction mixture using a mixture of hexane–benzene (1:2) gave the *title compound* **2f** (146 mg, 0.82 mmol, 20%), m.p. 37–38 °C (from hexane) (Found: C, 53.9; H, 3.3; N, 15.8. $C_8H_6N_2OS$ requires C, 53.92; H, 3.39; N, 15.72%); ν_{max}(KBr)/cm^{-1} 3600–3000 (OH), 1619, 1580, 1502, 1483, 1461, 1440, 1370, 1300, 1250, 1195, 1179, 1150, 1106, 1034, 932, 875, 829, 803, 790, 768, 755, 520 and 500; δ_H(60 MHz; $CDCl_3$) 7.12–8.34 (5 H, m, Ph and OH) and 9.26 (1 H, s, N=CH); *m/z* 178 (31.1%, M$^+$), 176 (100), 151 (19.6, M − HCN), 119 (4.5, M − HCNS) and 102 (21.2 M − HCNS − OH).

3-(m-*Hydroxyphenyl*)-1,2,5-*thiadiazole* **2g**. A mixture of *m*-hydroxyacetophenone oxime **1g** (606 mg, 4.01 mmol) and S_4N_4 (819 mg, 4.44 mmol) in *p*-dioxane was refluxed for 36 h. Chromatography of the reaction mixture using a mixture of hexane–ethyl acetate (1:3) gave a mixture, which was rechromatographed with a mixture of hexane–ethyl acetate (4:1) to give the *title compound* **2g** (291 mg, 1.63 mmol, 41%), m.p. 92–93 °C (from CCl_4) (Found: C, 53.9; H, 3.4; N, 15.7%); ν_{max}(KBr)/cm^{-1} 3600–3000 (OH), 1619, 1596, 1519, 1465, 1449, 1416, 1378, 1335, 1314, 1251, 1215, 1161, 1091, 1084, 998, 965, 889, 867, 841, 796, 705, 683, 649, 521 and 494; δ_H(60 MHz; $CDCl_3$) 6.97–7.76 (5 H, m, Ph and OH) and 8.83 (1 H, s, N=CH); *m/z* 178 (100%, M$^+$), 151 (66.6, M − HCN), 119 (50.0, M − HCNS) and 91 (11.7).

3-(2-*Thienyl*)-1,2,5-*thiadiazole* **2i**. A mixture of 2-acetylthiophene oxime **1i** (566 mg, 4.01 mmol) and S_4N_4 (1.294 mg, 7.02 mmol) in *p*-dioxane was refluxed for 36 h. After the solvent was removed under reduced pressure, the residue was dissolved in acetone (20 cm^3). Filtration of acetone-insoluble material, followed by evaporation of the solvent, gave a residue, which was repeatedly chromatographed using a mixture of hexane–benzene (3:1) to give the title compound **2i** (296 mg, 1.76 mmol, 44%) as yellow crystals, m.p. 36 °C (from hexane) (lit.,[8] 38–39 °C); ν_{max}(film)/cm^{-1} 3100, 3059, 1549, 1538, 1471, 1422, 1344, 1231, 1220, 1089, 1064, 894, 850, 848, 830, 785, 775 and 709; δ_H(60 MHz; $CDCl_3$) 7.21–7.91 (3 H, m, Ph) and 8.98 (1 H, s, N=CH).

8H-*Indeno*[1,2-c][1,2,5]*thiadiazole* **2j**. A mixture of (*E*)-indan-1-one oxime **1j** (598 mg, 4.06 mmol) and S_4N_4 (844 mg, 4.58 mmol) in *p*-dioxane was refluxed for 24 h. Filtration of the dark reaction mixture, followed by evaporation of the solvent, gave a residue, which was repeatedly chromatographed using light petroleum (30–60 °C) followed by benzene to give the title compound **2j** (233 mg, 1.34 mmol, 33%), m.p. 69–70 °C (from hexane–CCl_4) (lit.,[21] 72–74 °C); δ_H(80 MHz; $CDCl_3$) 3.83 (2 H, s, CH_2) and 7.36–7.98 (4 H, m, Ph).

1,3-*Bis*-[3-(1,2,5-*thiadiazolo*)]*benzene* **2k**. A mixture of 1,3-diacetylbenzene dioxime **1k** (588 mg, 2.06 mmol) and S_4N_4 (1.337 mg, 7.26 mmol) in *p*-dioxane was refluxed for 60 h. The solution turned gradually dark red and dark solids were formed. The reaction mixture was occasionally swirled so as not to become stiff on the wall of the flask. After removal of the solvent, the residue was chromatographed using a mixture of benzene–chloroform (1:1) to give the *title compound* **2k** (193 mg, 0.78 mmol, 26%), m.p. 90–91 °C (from hexane–$CHCl_3$) (Found: C, 48.8; H, 2.4; N, 22.8. $C_{10}H_6N_4S_2$ requires C, 48.76; H, 2.46; N, 22.75%); ν_{max}(KBr)/cm^{-1} 1461, 1436, 1364, 1329, 1310, 1270, 1218, 1098, 968, 921, 896, 882, 850, 841, 800, 734, 696 and 524; δ_H(80 MHz; $CDCl_3$) 7.54–8.65 (4 H, m, Ph) and 8.99 (2 H, s, 2 × N=CH); *m/z* 246 (100%, M$^+$), 219 (43.7, M − HCN), 187 (25.8, M − HCNS), 160 (69.2, M − 2 HCN − S), 128 (18.3, M − 2 HCNS) and 102 (15.7, M − 2 HCNS − CN).

1,4-*Bis*-[3-(1,2,5-*thiadiazolo*)]*benzene* **2l**. A mixture of 1,4-diacetylbenzene dioxime **1l** (583 mg, 3.03 mmol) and S_4N_4 (1.296 mg, 7.03 mmol) in *p*-dioxane was refluxed for 60 h. Work-up as for the isomer **2k** gave the *title compound* **2l** (283 mg, 1.15 mmol, 38%), m.p. 204–205 °C (from CCl_4) (Found: C, 48.8; H, 2.3; N, 22.7%); ν_{max}(KBr)/cm^{-1} 1468, 1421, 1346, 1314, 1277, 1229, 1120, 1086, 927, 881, 841, 790, 700, 675 and 534; δ_H(80 MHz; $CDCl_3$) 8.14 (4 H, s, Ph) and 8.97 (2 H, s, N=CH); *m/z* 246 (100%, M$^+$), 219 (37.4, M − HCN), 187 (29.9, M − HCNS), 160 (69.2, M − HCNS − HCN), 128 (37.4, M − 2 HCNS) and 102 (21.7, M − 2 HCNS − CN).

2,6-*Bis*-[3-(1,2,5-*thiadiazolo*)]*pyridine* **2m**. A mixture of 2,6-diacetylpyridine dioxime **1m** (596 mg, 3.08 mmol) and S_4N_4 (1.337 mg, 7.26 mmol) in *p*-dioxane was refluxed for 72 h. Work-up as for compound **2k** gave the *title compound* **2m** (368 mg, 1.49 mmol, 48%) as a solid, m.p. 179–180 °C (from CCl_4) (Found: C, 43.6; H, 2.1; N, 28.3. $C_9H_5N_5S_2$ requires C, 43.71; H, 2.04; N, 28.32%); ν_{max}(KBr)/cm^{-1} 1588, 1569, 1452, 1411, 1350, 1323, 1311, 1260, 1229, 1218, 1157, 1107, 1079, 998, 932, 909, 843, 834, 819, 801, 787, 738, 702, 648 and 521; δ_H(80 MHz; $CDCl_3$), 7.88–8.31 (3 H, m, ArH) and 9.41 (2 H, s, 2 × N=CH); *m/z* 247 (100%, M$^+$), 246 (13.5, M − 1), 220 (M − HCN), 189 (M − HCNS), 162 (14.0, M − HNCS − HCN) and 130 (24.3, M − 2 HCNS).

4,5-*Dihydrobenzo*[1,2-c;3,4-c']*bis*[1,2,5]*thiadiazole* **5**. (a) A mixture of cyclohexanone oxime **4** (462 mg, 4.08 mmol) and S_4N_4 (825 mg, 4.48 mmol) in *p*-dioxane was refluxed for 4 h. The mixture was worked up as for compound **2a**. Column chromatography using a mixture of hexane–benzene (1:1) gave S_4N_4 (87 mg, 0.47 mmol, 10%). Continuous elution with benzene gave the *title compound* **5** (49 mg, 0.25 mmol, 6%), m.p. 144–145 °C (from hexane) (Found: C, 36.8; H, 2.1; N, 28.5. $C_6H_4N_4S_2$ requires C, 36.72; H, 2.05; N, 28.55%); ν_{max}(KBr)/cm^{-1} 2920, 1503, 1445, 1429, 1418, 1384, 1201, 1170, 1040, 1013, 980, 877, 828, 807, 781 and 753; δ_H(80 MHz; $CDCl_3$) 3.43 (4 H, s, 2 × CH_2); δ_C(50.3 MHz; $CDCl_3$) 25.32, 151.25 and 161.48; *m/z* 196 (100%, M$^+$), 163 (16.6), 149 (6.0), 137 (6.7) and 72 (17.8).

(b) A mixture of compound **4** (469 mg, 4.14 mmol) and S_4N_4 (859 mg, 4.66 mmol) in toluene (20 cm^3) was refluxed for 4 h. The solvent was removed under reduced pressure and the residue was dissolved in chloroform (20 cm^3). After chloroform-insoluble material had been filtered off, the filtrate was concentrated to dryness. The residue was chromatographed using hexane to give a mixture of sulfur, S_4N_4, and oily liquids. Elution next with benzene afforded the title compound **5** (57 mg, 0.29 mmol, 7%). Rechromatography of the mixture of sulfur, S_4N_4, and oily liquids with hexane, followed by carbon tetrachloride, gave sulfur and S_4N_4, respectively. After removal of a purple band by elution with a mixture of hexane–benzene (3:1), an oily liquid (168 mg) was isolated using the same solvents (1:1); ν_{max}(film)/cm^{-1} 3213, 2941, 2859, 1446, 1430, 1414, 1344, 1120, 808, 639 and 611; δ_H(80 MHz; $CDCl_3$) 1.53–1.62 (m), 2.03–1.81 (m) and 3.04–2.88 (m); HPLC (Column μBondapak C_{18} 10 μm, 7.8 mm × 300 mm, flow rate 1.0 cm^3 min^{-1}, solvent MeCN) showed two peaks whose retention times were 6.52 min (48%) and 6.96 min (52%).

Reaction of o-*Methoxyacetophenone Oxime* **1h** *with* S_4N_4.—A mixture of *o*-methoxyacetophenone oxime **1h** (675 mg, 4.09 mmol) and S_4N_4 (821 mg, 4.46 mmol) in *p*-dioxane (20 cm^3) was refluxed for 48 h. Chromatography of the reaction mixture with benzene afforded a mixture (184 mg), which was rechromatographed using hexane, followed by carbon tetrachloride, to give *o*-methoxyacetophenone (23 mg, 3%). Continuous elution with a mixture of hexane–benzene (1 : 3) afforded unknown mixtures (139 mg).

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References

1 *Gmelin Handbook of Inorganic Chemistry*, Sulfur-Nitrogen Compounds, Part 2 B, ed. B. Heibel, Springer Verlag, Berlin, 1984, 8th edn., ch. 5, p. 127.
2 J. Cho and K. Kim, *J. Heterocycl. Chem.*, 1992, **29**, 1433.
3 P. J. Dunn and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1989, 2485.
4 S. Mataka, K. Takahashi, S. Ishi-i and M. Tashiro, *J. Chem. Soc., Perkin Trans. 1*, 1979, 2905.
5 J. H. Smith and E. T. Kaiser, *J. Org. Chem.*, 1974, **39**, 728.
6 V. Bertini and A. De Munno, *Gazz. Chim. Ital.*, 1967, **97**, 1614.
7 S. Mataka, K. Takahashi, Y. Yamada and M. Tashiro, *J. Heterocycl. Chem.*, 1979, **16**, 1009.
8 S. Mataka, K. Takahashi and M. Tashiro, *Oppi. Brief.*, 1985, **17**, 152 (*Chem. Abstr.*, 1985, **102**, 185013x).
9 E. O. Sherman, Jr., S. M. Lambert and K. Pilgram, *J. Heterocycl. Chem.*, 1974, **11**, 763.
10 I. I. Grandberg, A. N. Kost and L. S. Yaguzhinskii, *Zh. Obshch. Khim.*, 1959, **29**, 2537 (*Chem. Abstr.*, 1960, **54**, 11000e).
11 S. Mataka, A. Hosoki, K. Takahashi and M. Tashiro, *J. Heterocycl. Chem.*, 1980, **17**, 1681.
12 S. Mataka, K. Takahashi, S. Shiwaku and M. Tashiro, *J. Chem. Soc., Chem. Commun.*, 1983, 1136.
13 J. C. Craig and A. R. Naik, *J. Am. Chem. Soc.*, 1962, **84**, 3410.
14 S. Mataka, K. Takahashi and M. Tashiro, *J. Heterocycl. Chem.*, 1977, **14**, 963.
15 V. Bertini, A. De Munno and A. Marraccini, *J. Org. Chem.*, 1972, **37**, 2587.
16 S. Mataka, K. Takahashi, Y. Ikezaki, T. Hatta, A. Torii and M. Tashiro, *Bull. Chem. Soc. Jpn.*, 1991, **64**, 68.
17 B. S. Furniss, A. J. Hannaford, P. W. G. Smith and A. R. Tatchell, *Vogel's Textbook of Practical Organic Chemistry*, Longman Scientific Technical, London, 5th edn., 1989, p. 1259.
18 *Dictionary of Organic Compounds*, ed. J. Buckingham, Chapman and Hall, London, 5th edn., 1982; (*a*) vol.1, p. 18; (*b*) vol. 5, p. 4663; (*c*) vol. 5, p. 4606; (*d*) vol. 1, p. 137; (*e*) vol. 1, p. 138; (*f*) vol. 3, p. 2982; (*g*) vol. 2, p. 1518; (*h*) vol. 2, p. 1519; (*i*) vol. 2, p. 1370.
19 O. Meth-Cohn and B. Narine, *Synthesis*, 1980, 133.
20 G. W. Buchanan and B. A. Dawson, *Can. J. Chem.*, 1978, **56**, 2200.
21 S. Mataka, A. Hosoki, K. Takahashi and M. Tashiro, *Synthesis*, 1982, 976.

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