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A new simple synthesis of *cis*- and *trans*-3,5-di-*tert*-butyl-3,5-diaryl-1,2,4-trithiolanes from ketones and tetraphosphorus decasulfide

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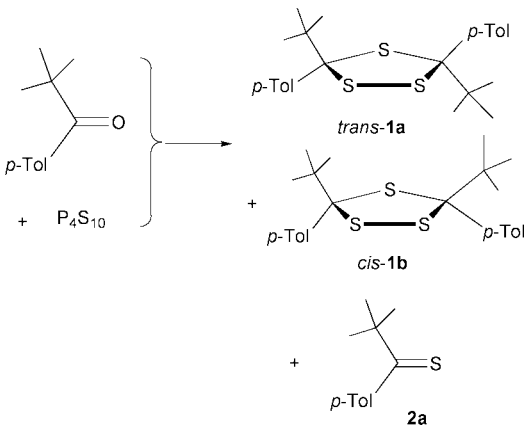
The reaction of pivalophenones with tetraphosphorus decasulfide afforded *cis*- and *trans*-3,5-di-*tert*-butyl-3,5-diaryl-1,2,4-trithiolanes, which equilibrated to give other isomers in refluxing toluene *via* thiopivalophenones and thiopivalophenone *S*-sulfides.

1,2,4-Trithiolanes (**1**), some of which have been obtained from natural products, are well-known.[1] Methods for their synthesis include: reaction of thiobenzophenone with *o*-chloranil,[2] reaction of thiobenzophenones with 1,1-diphenylethylene sulfide,[3] reaction of thiones with Lowesson reagents,[4] reaction of dialkyl ketones with hydrogen sulfide elemental sulfur, and amines,[5] and fragmentation of 1,2,3-thiadiazoles.[6] Recently, Senning and co-workers reported that reaction of α-chlorosulfenyl disulfides with morpholine afforded the corresponding dispirotrithiolanes.[7] However, there are only a few reports on the synthesis of trithiolanes from ketones using thiation reagents although it is well known that the reaction of ketones with tetraphosphorus decasulfide (P_4S_{10}) affords the corresponding thioketones.[8] We have investigated the synthesis of trithiolanes from ketones using P_4S_{10} as a thiation reagent and report herein the isolation and X-ray crystallographic analysis of *cis*- and *trans*-**1** from P_4S_{10} and their thermal isomerization.

Treatment of 4-methylpivalophenone with P_4S_{10} in refluxing pyridine for 48 h resulted in the formation of *trans*-3,5-di-*tert*-butyl-3,5-di-*p*-tolyl-1,2,4-trithiolane (*trans*-**1a**), *cis*-3,5-di-*tert*-butyl-3,5-di-*p*-tolyl-1,2,4-trithiolane (*cis*-**1a**), and 4-methylthiopivalophenone (**2a**) in 13, 35, and 23% yields, respectively. Refluxing for 72 h resulted in the formation of *cis*-**1a** in 35 % yield along with *trans*-**1a** (24%) and **2a** (16%) (Scheme 1).

The structures *cis*-**1a** and *trans*-**1a** were confirmed by NMR and elemental analysis. Table 1 lists the ^{1}H NMR and ^{13}C NMR data for *cis*- and *trans*-**1a**. The chemical shift of the *tert*-butyl group of trans-**1a** is higher than that of *cis*-**1a**, whereas chemical shifts of the aromatic groups of trans-**1a** are lower than those of *cis*-**1a**. This observation suggests that each aromatic group of *cis*-**1a** was on the other aromatic plane whereas the *tert*-butyl group of *trans*-**1a** was on the aromatic plane.



Scheme 1

Both structures were confirmed by single crystal X-ray crystallographic analysis (Fig. 1)[9]: no unusual bond lengths or angles are observed in the 1,2,4-trithiolane rings. The trithiolane rings of both products have similar conformations to other trithiolanes. The C–S bond lengths of the trithiolane rings are between 1.796 and 1.875 Å—longer than normal (1.763–1.767 Å)[6] because the trithiolane rings are compressed by bulky *tert*-butyl groups. However, the S–S bond lengths (2.027 Å for *cis*-**1a** and 2.016 Å for *trans*-**1a**) are shorter than the one reported by Senning *et al.* (2.0345 Å).[7] As suggested by their NMR spectra, the aromatic groups of *cis*-**1a** were out of plane whereas the *tert*-butyl group of *trans*-**1a** was on the aromatic plane.

Other reactions were similarly carried out. The results are shown in Table 2.

More than three decades ago, Elam and Davis reported the synthesis of dimethylthioketene dimer by the reaction of tetramethylcyclobutane-1,3-dione with tetraphosphorus decasulfide. They isolated the corresponding trithiolane as a side product (2.8%).[8] However, they did not apply the general synthesis of **1** from ketones. The reaction of pivalophenone with P_4S_{10} generally afforded thiopivalophenone in good yield.[10] The present reaction is the first practical method on the synthesis of **1** from ketones by using P_4S_{10}.

Thiocarbonyl *S*-sulfides (thiosulfines) are well-known to exhibit high reactivity such as dienophile-like behavior, for example, and can add to a variety of thiones to give **1**. 3,3,5,5-Tetraaryl-1,2,4-trithiolanes are thermally unstable and dissociate into thiocarbonyl *S*-sulfides and thiobenzophenone in refluxing chloroform.[3] Since *cis*- and *trans*-**1** were isolated, the thermal behavior of these isomers was investigated. A solution of *cis*-**1a** in deuterated toluene was heated at 110 °C for 72 h. The ^{1}H NMR spectroscopic analysis of the solution revealed that *cis*-**1a** gradually converted to *trans*-**1a** (26%), along with **2a** (44%), whereas *cis*-**1** a was recovered in 25% yield. While *trans*-**1a** also converted to *cis*-**1a**, the rate of conversion was low. After being heated at 110 °C for 72 h, 66% of *trans*-**1a** still remained, suggesting that *trans*-**1a** is more stable than the corresponding *cis*-isomer. The most straightforward explanation for the conversion of *cis*-**1a** to *trans*-**1a** involves the isomerization of *cis*-**1a** to the thiocarbonyl *S*-sulfide (**3a**) and **2a** followed by recombination *via* 1,3-dipolar cycloaddition between **3a** and **2a** (Scheme 2).

Table 1 Spectral data of *cis*- and *trans*-**1a**

	^{1}H NMR	^{13}C NMR
trans-**1a**	1.04 (s, 18H, *t*-Bu), 2.35 (s, 6H, ArMe), 7.10 (d, 4H, *J* = 8.0 Hz, Ar), 7.81 (d, 4H, *J* = 8.0 Hz, Ar)	20.93, 29.78, 40.71, 100.65, 127.11, 130.84, 136.15, 140.11
cis-**1a**	1.21 (s, 18H, *t*-Bu), 2.20 (s, 6H, ArMe), 6.81 (d, 4H, *J* = 8.2 Hz, 7.40 (d, 4H, *J* = 8.2 Hz, Ar)	20.75, 28.81, 41.96, 97.76, 126.52, 130.39, 135.74, 137.96

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Table 2 Reaction of ketones with tetraphosphorus decasulfide

Ketone		Conditions			Products (Yields/%)		
					Trithiolane		
R′	R″	Temp./°C	Solvent	Time/h	*cis*	*trans*	Thioketone **2**
t-Bu	*p*-Tol	110	Pyridine	24	**1a** 22	3	**2a** 52
t-Bu	*p*-Tol	110	Pyridine	96	**1b** 34	35	**2a** 28
t-Bu	Ph	110	Pyridine	48	**1b** 21	8	**2b** 30
t-Bu	*p*-$PhOC_6H_4$	110	Pyridine	48	**1c** 19	10	**2c** 35
Adamantane-2-one		110	Pyridine	48	**1d**	45	**2d** 13

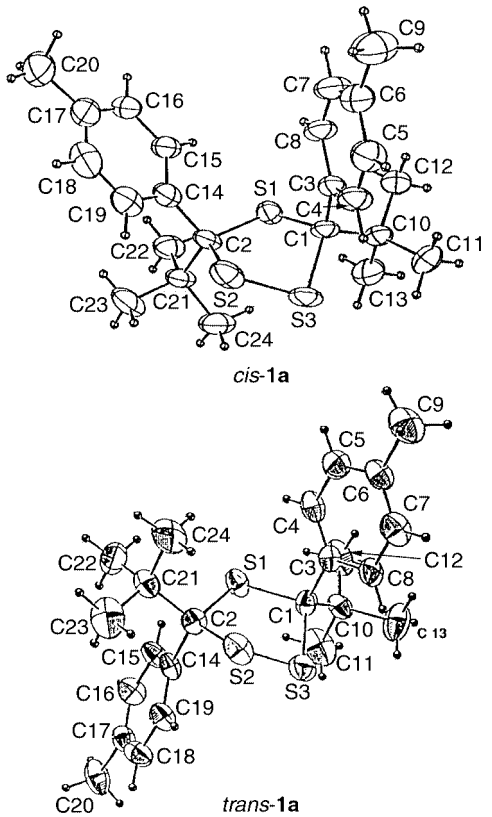
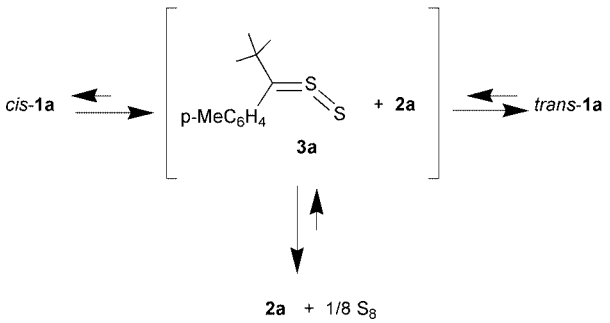


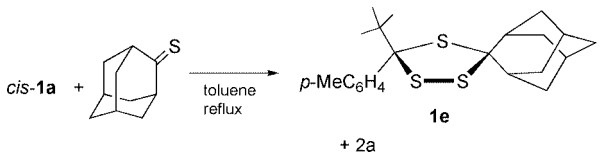
Fig. 1 X-ray crystallographic structures of *cis*- and *trans*-**1a**. Selected data for cis-**1a**. Bond lengths: C1–S1 1.864(4); C1–S3 1.841 (5); S1–C2 1.855(5); C2–S2 1.861(4); S2–S3 2.037 Å. Bond angles: C1–S1–C2 104.0(2); S3–S2–C2 99.5 (2); S2–S3–C1 94.9(2); S1–C1–S3 104.0(2); S1–C2–S2 107.1(2)°. Selected data for *trans*–**1a**. Bond lengths: C1–S1 1.870(8); C1–S3 1.796 (8); S1–C2 1.854 (8); C2–S2 1.840(8); S2–S3 2.016 (3) Å. Bond angles: C1–S1–C2 102.8(4); S3–S2–C2 96.6 (3); S2–S3–C1 95.5(3); S1–C1–S3 106.4(4); S1–C2–S2 106.5(4)°.



Scheme 2

When the reaction was carried out in the presence of adamantane-2-thione (2 eq.), the corresponding cycloadduct (**1e**) was obtained in 67% yield along with recovered *cis*-**1a** (15 %) and **2a** (70%) (Scheme 3).[11]

The difference in stability between *cis*- and *trans*-**1** might be attributed to the difference in their steric hindrances. As can be



Scheme 3

seen in Figure 1, *cis*-**1a** is more crowded than the *trans* isomer. In fact, Senning *et al.* have reported that the reaction of thiosulfenyl chloride with morpholine afforded mainly the corresponding *trans*-trithiolane, suggesting that *cis*-trithiolane is generally unstable and gradually converts into the more stable *trans*-isomer.[7]

In summary, we have isolated and characterized *cis*- and *trans*-**1** by the reaction of pivalophenones with P_4S_{10}. Both isomers interconvert in refluxing toluene. The intermediate **3** was trapped by the reaction with adamantane-2-thione to afford unsymmetrical **1**.

Notes and references

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9 Crystal data for $C_{24}H_{32}S_3$ *cis*-**1a**: M = 416.71, a = 6.606(1), b = 10.981(3), c = 16.559(3) Å, α = 88.2(2), β = 79.16(1), γ = 76.09(2)°, T = 297 K, space group $P\bar{1}$ (No. 2), Z = 2, μ(Cu-Kα) = 29.4 cm^{-1}, 4183 reflections measured, 4036 unique (R_{int} = 0.072). 3298 reflections ($|F_o| > 3.0\sigma(F_o)$) were used in all calculations. The final R and wR were 0.090 and 0.116 respectively. Crystal data for $C_{24}H_{32}S_3$ *trans*-**1a**: M = 416.71, a = 13.987(2), b = 17.561(3), c = 9.498(3) Å, β = 79.16(1)°, T = 297 K, space group $P2_1/a$ (No. 14), Z = 4, μ = (Cu-Kα) = 29.1 cm^{-1}, 4443 reflections measured, 4126 unique (R_{int} = 0.062). 1753 reflections ($|F_o| > 3.0\sigma(F_o)$) were used in all calculations. The final R and wR were 0.078 and 0.073 respectively. Both isomers were recrystallised from methanol. The structure was solved using direct methods and refined by full-matrix least-squares on F. CCDC 182/1714.

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11 Compound **1e**: mp 152.3–152.8 °C. ^{1}H NMR ($CDCl_3$) δ = 1.18 (s, 9H, *t*-Bu), 1.63–2.49 (m, 14H, Ad-H), 2.33 (s, 3H, Me), 7.07 (d, 2H, J = 4 Hz, Ar), 7.78 (d, 2H, J = 4 Hz, Ar). ^{13}C NMR ($CDCl_3$) δ = 20.90, 26.65, 29.44, 34.97, 36.53, 37.73, 38.78, 39.71, 40.20, 90.68, 98.82, 126.87, 130.52, 136.04, 139.37.