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The Novel and Efficient Methods for the Synthesis of Symmetrical Trisulfides.

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Abstract: We have developed a convenient methods for the synthesis of symmetrical trisulfides under mild conditions in very good yields. The described methods are based on the straightforward preparation of 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinane-2-disulfanyl derivatives from readily available 5,5-dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphorinane or bis(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl) disulfide. The symmetrical trisulfides can be obtained from aliphatic, aromatic thiols and L-cysteine derivatives as well.

Key words: symmetrical trisulfides, thiols, sulfenyl bromides, L-cysteine.

The biological importance of the sulfur-sulfur bond comprises the organic trisulfides as well. Several trisulfides have been isolated from natural sources [1] especially from plants in the onion family (genus Allium). The trisulfide functionality was also found in the tumor inhibitors calicheamicin [2] and esperamicin [3] the members of the enediyne group of antibiotics. The preparation of symmetrical, acyclic trisulfides is well documented.[4] The most common methods for obtaining trisulfides include the reaction of thiols with sulfur dichloride,[5] the coupling of alkyl halides with sodium trisulfide,[6] the reaction of thiols or disulfides with sulfur.[7] Thioalkylation of various thiosulfenate species can also produce trisulfides. The most suitable substrates include Bunte salts,[8] metal sulfides,[9] and thiosulfenyl chloride.[10] The latest one can be used for preparation of unsymmetrical trisulfides. Other practical procedures involve the reduction of thiosulfonates and disulfonyl sulfides with phosphines,[11] sulfur insertion reactions into thiosulfinates, thiosulfonates,[12] and disulfides,[13] alkoxide decomposition of sulfenylthiocarbonates,[14] and reactions of thiols with 1,1'-thiobis(benzimidazole) [15] or diimidazolylsulfide.[16]

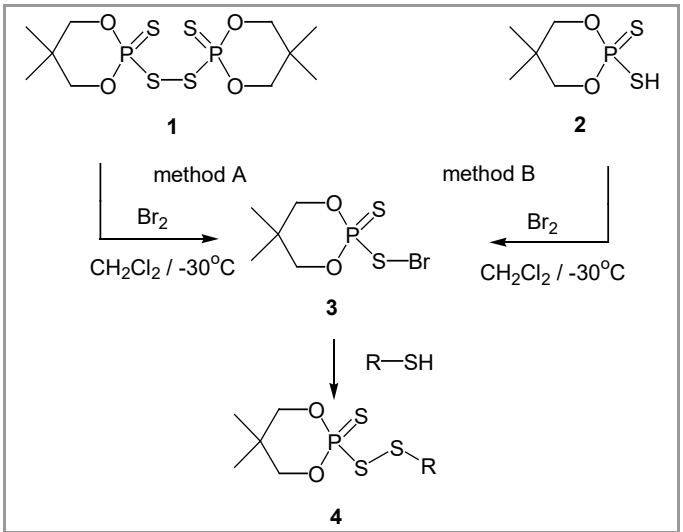
The preparation of unsymmetrical trisulfides is not usually trivial. There are known procedures based on the coupling of chlorodisulfides with *N*-arylamidothiosulfites [17] or thiols,[18] the sequential coupling of two thiols using sulfur dichloride.[19] Other procedures involve the desulfurization of unsymmetrical dialkanesulfonic thioanhydrides,[11] or require the use of unstable in most cases hydrodisulfides.[20]

Although the preparation of symmetrical trisulfides is straightforward and well documented, the synthesis of these compounds is in fact more complex. Most of the above methods suffer from either moderate yields or the formation of undesirable polysulfides side products. The removal of these impurities in most cases is not possible. The best method of purification is crystallization, but it can be applied only for solid trisulfides. Other methods require the multi step synthesis of appropriate precursors or using freshly distilled sulfur dichloride.[5] Additionally, the presence of functional groups is very often compromised by the used reagents and conditions of the reaction.

We have previously demonstrated the preparation functionalized unsymmetrical molecules, such as dialkyl disulfides, alkyl-aryl disulfides,[21] "bioresistant" disulfides,[22] unsymmetrical disulfides based on L-cysteine and L-cystine derivatives,[23] and diaryl disulfides.[24] The excellent results encouraged us to extend the strategy to the preparation of symmetrical trisulfides based on the readily available 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinane-2-disulfanyl derivatives.

Treatment of the stable and readily available bis(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl) disulfide **1** (method A) or 5,5-dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphorinan **2** (method B) with bromine at –30 ºC quantitatively affords 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinane-2-sulfenyl bromide **3** (Table 1).

Table 1 Synthesis of 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl-disulfanyl derivatives **4**

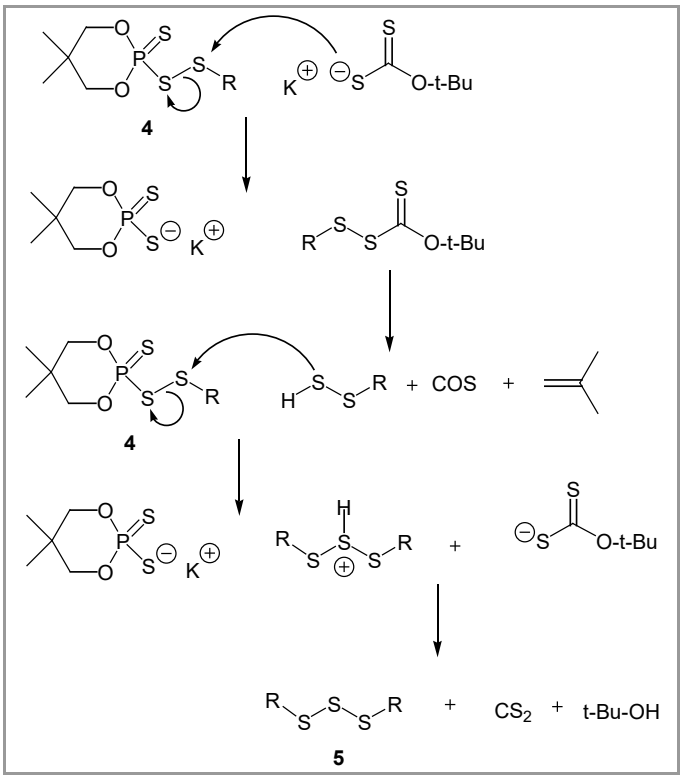


Entry	R	4	Yield (%) by Method A	Yield (%) by Method B
1	$-(CH_2)_{11}CH_3$	**4a**	100	99
2	$-(CH_2)_{11}OH$	**4b**	95	93
3	$-(CH_2)_{10}CO_2H$	**4c**	92	94
4	$-(CH_2)_2OH$	**4d**	95	92

5	-(*R*)-$CH_2CH(NHBoc)CO_2Et$	**4e**	98	94
6	4-Tol	**4f**	95	91

Subsequent treatment, without prior isolation, of sulfenylu bromide **3** with variety of thiols provides the corresponding 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinane-2-disulfanyl derivatives **4a-f**, which can be isolated in very good yields (Table 1, entries 1-6). These compounds are stable at room temperature for several months; decomposition by moisture or formation of symmetrical disulfides was not observed.

The reaction of disulfide **4a** with one equivalent of potassium *O*-*tert*-butyl dithiocarbonate was intended to prepare *tert*-butyl dodecylsulfenyldithiocarbonate ($CH_3(CH_2)_{11}SSCSOtBu$) , convenient precursor of dodecyl hydrodisulfide. Surprisingly, when above reagents were allowed to react in the methanol at room temperature, both dodecyl tetra- and trisulfide were produced in a ratio of approximately 1:8. When the same reaction of **4a** was repeated with 1.1 equivalent of potassium *O*-*tert*-butyl dithiocarbonate in methanol at 0 ºC until **4a** was consumed (followed by TLC, usually it takes ca. 30 min.), then di-dodecyl trisulfide **5a** was isolated in 90% yield (Table 2, method A, entry 1). The mechanism of the reaction may be formulated by nucleophilic attack of the *O*-*tert*-butyl dithiocarbonate anion on the sulfur in the compound **4** to displace the phosphorodithioic anion and produce *tert*-butyl sulfenyldithiocarbonate. The latter then is decomposed to hydrodisulfie, which reacts with another molecule of **4** to give trisulfide (Scheme 1).

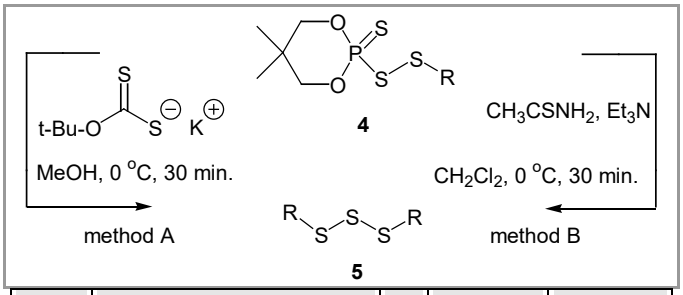


Scheme 1 The proposed mechanism of trisulfides **5** formation from potassium *O*-*tert*-butyl dithiocarbonate.

The above mechanism explains the 1:1 ratio of starting materials and may suggest that the trisulfide formation by tert-butoxide decomposition of sulfenylthiocarbonates proceed by similar mechanistic paths.[14] However, decomposition of *tert*-butyl sulfenyldithiocarbonate derivatives to hydrodisulfides and their reactions with **4** require further investigation.

Compounds **4b-f** were treated with potassium *O*-*tert*-butyl dithiocarbonate to examine the scope and limitation of this method for the preparation symmetrical trisulfides **5** (table 2, method A, entries 2-6).

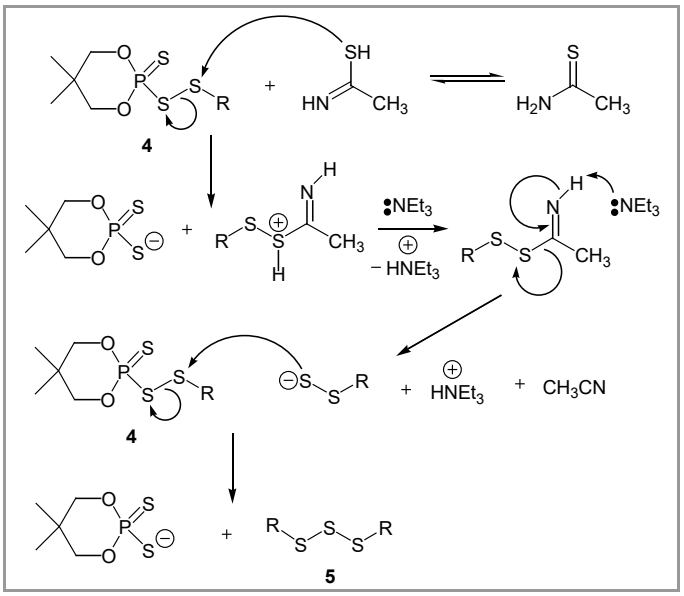
Table 2 Synthesis of symmetrical trisulfides **5**



Entry	R	**5**	Yield (%) by Method A	Yield (%) by Method B
1	$-(CH_2)_{11}CH_3$	**5a**	90	95
2	$-(CH_2)_{11}OH$	**5b**	84	94
3	$-(CH_2)_{10}CO_2H$	**5c**	92	89
4	$-(CH_2)_2OH$	**5d**	81	91
5	-(*R*)-$CH_2CH(NHBoc)CO_2Et$	**5e**	92	94
6	4-Tol	**5f**	87	94

As can be seen from the above data, the presence of hydroxy, carboxyl, ester and protected amino groups did not disturb the course of the reaction and corresponding trisulfides **5** were isolated in very good yield 81-92%. Although the yields are very high, much more important is the exclusive formation of trisulfide without the formation of undesirable polysulfides side products.

The reaction of disulfides **4** with 0.55 equivalent of commercially available thioacetamide in CH_2Cl_2 at 0 ºC in the presence of Et_3N afforded symmetrical trisulfide **5** in very high yield 89-95% (Table 2, method B, entries 1-6). This method is also very effective and exclusive formation of trisulfides **5** was observed. The proposed mechanism is presented in scheme 2.



Scheme 2 The proposed mechanism of trisulfides **5** formation from thioacetamide.

The ratio of reagents, isolation of phosphorodithioic triethylammonium salt and trisulfide **5** are with agreement to presented above mechanism.

As shown in Table 2, the same trisulfide can be obtained by two different methods. Both approaches gave product **5** in very high yield. Moreover, it seems that presence of additional functional groups did not affect the formation of trisulfides **5**. The success of the developed protocols depends on the very fast formation of **5** from **4** through the hydrodisulfide intermediate so that formation of undesirable polysulfides side products was avoided. All trisulfides **2** in Table 2 were stable at room temperature for several weeks. However, on the exposure to light the aromatic compound **5f** was converted to the mixture of polysulfides (from disulfides to pentasulfide). Similar behavior was observed previously by Harpp and coworkers.[5a] The presence of air atmosphere or moisture did not affect the stability of trisulfides **5**.

In conclusion, all reactions from methods A and B took place under mild conditions without any additional catalysts or reagents, except for the commercially available Et_3N or thioacetamide. Moreover, commercial grade solvents were used without purification and the reactions were performed under air atmosphere. The symmetrical trisulfides can be obtained from aliphatic, aromatic thiols and L-cysteine derivatives as well. The presence of functional groups: amino, hydroxy, or carboxyl did not disturb the course of the reaction. The advantages of these new methods are the easily accessible starting materials, convenient manipulation, short reaction time, very high purity and yields. From this point of view, presented above methods synthesis of symmetrical trisulfides seems to be currently one of the most versatile and convenient approaches to preparation of functionalized trisulfides.

1-Dodecanethiol, 11-sulfanylundecanol, 11-sulfanylundecanoic acid, 2-sulfanylethanol, 4-methylbenzenethiol, and thioacetamide are commercially available from Aldrich. *N*-(*tert*-butoxycarbonyl)-L-cysteine ethyl ester,[25] bis(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl) disulfide (**1**),[26] 5,5-dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphorinan (**2**)[26] and potassium *O*-*tert*-butyl dithiocarbonate [27] were synthesized by described procedures. Commercial grade CH_2Cl_2 and methanol were used for synthesis of trisulfides **5** from **4**. Melting points are uncorrected. NMR spectra were recorded on a Varian Gemini 500 MHz or 200 MHz spectrometer. The residual solvent peak was used as internal reference ($CDCl_3$: δ = 7.26 for ^1H, δ= 77.0 for ^{13}C); ^{31}P NMR used an external standard as reference (85% H_3PO_4: δ = 0). ESI-MS spectra were recorded on a Mariner PerSeptve Biosystem. Column chromatography was performed with silica gel 60 (230–400 mesh, Merck). Preparative TLC chromatography was performed with silica gel Polygram SIL G/UV254 (Macherey-Nagel).

11-[(5,5-Dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl)disulfanyl]undecane-1-ol (4b); Typical Procedure (method A)

Br_2 (0.96 g, 6.0 mmol) was added to a soln of **1** (2.76 g, 7.0 mmol) in anhyd CH_2Cl_2 (50 mL) at –30 °C and under N_2. After 15 min, a soln of 11-sulfanylundecanol (2.25 g, 11 mmol) in anhyd CH_2Cl_2 (5 mL) was added. Then the mixture was stirred at r.t. for 30 min, diluted with CH_2Cl_2 (50 mL), washed with H_2O (50 mL), dried ($MgSO_4$), filtered, and evaporated under vacuum. The residue was purified by column chromatography (silica gel, CH_2Cl_2); this yielded **4b**.

Yield: (4.42 g, 95%); white solid; mp 40–42 °C.

IR (cm^{-1}, KBr): ν = 3368 (m), (OH), 2970 (m), 2925 (s), 2856 (w), (CH), 1048 (s), 995 (s) (POC), 684 (s) (P=S).

^1H NMR (500MHz, $CDCl_3$): δ = 1.06 (s, 3H, CH_3), 1.22 (s, 3H, CH_3), 1.23-1.45 (m, 14H, CH_2), 1.55-1.62 (m, 2H, CH_2), 1.68-1.76 (m, 2H, CH_2), 3.02 (t, J = 7.3 Hz, 2H, $PSSCH_2$), 3.66 (t, J = 6.6 Hz, 2H, OCH_2), 4.08-4.18 (m, 4H, $POCH_2$).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 77.5 (d, $^2J_{P-C}$ = 9.1 Hz), 63.0, 38.6, 32.7, 32.6 (d, $^3J_{P-C}$ = 7.1 Hz), 29.5, 29.4, 29.3, 29.0, 28.7, 28.3, 25.6, 21.9, 21.1. Expected 15, observed 14 signals.

^{31}P NMR (202 MHz, $CDCl_3$): δ = 86.67

HRMS (ESI): *m/z* [M + Na]+ calcd for $C_{16}H_{33}NaO_3PS_3$: 423.1227; found: 423.1229.

Compounds **4a**,[21] **4c-e** [23] and **4f** [24] were characterized previously.

11-[(5,5-Dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl)disulfanyl]undecan-1-ol (4b); Typical Procedure (Method B)

Br_2 (1.92 g, 12.0 mmol) was added to a soln of **2** (2.78 g, 14.0 mmol) in anhyd CH_2Cl_2 (50 mL) at –30 °C and

under N_2. After 15 min, a soln of 11-sulfanylundecanol (2.25 g, 11 mmol) in anhyd CH_2Cl_2 (5 mL) was added. Then the mixture was stirred at r.t. for 30 min, diluted with CH_2Cl_2 (50 mL), washed with H_2O (50 mL), dried ($MgSO_4$), filtered, and evaporated under vacuum. The residue was purified by column chromatography (silica gel, CH_2Cl_2); this gave **4b**.

Yield: (4.33 g, 93%); white solid; mp 40–42 °C.

Compounds **4a** and **4c-f** were prepared similarly from **2**, and the yields are reported in Table 1.

Symmetrical trisulfides 5 from 4a-f; General Procedure (Method A)

A soln of potassium *O-tert*-butyl dithiocarbonate (0.414 g, 2.2 mmol) in methanol (10 mL) was added to a soln of one of **4a-f** (2.0 mmol) in methanol at 0 °C under air atmosphere. The mixture was stirred at 0 °C for 30 min, and evaporated under vacuum. The residue was purified by column chromatography.

Di-dodecyl trisulfide (5a)

Chromatography (petroleum ether); yield: 90%; waxy white solid mp 15–16 °C

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.89 (t, *J* = 6.5 Hz, 6 H, CH_3), 1.15-1.45 (m, 36 H, CH_2), 1.64-1.84 (m, 4 H, CH_2), 2.88 (t, *J* = 7.3 Hz, 4 H, S-CH_2).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 38.9, 31.9, 29.6, 29.6, 29.5, 39.3, 29.2, 28.8, 28.5, 22.7, 14.1. Signals: expected, 12; observed, 11.

HRMS (ESI): *m*/*z* [M + H]+ calcd for $C_{24}H_{51}S_3$: 435.3153; found: 435.3157.

Bis(11-hydroxyundecyl) trisulfide (5b)

Chromatography ($CHCl_3$–MeOH, 25:1); yield: 84%; white solid mp 61–63 °C

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.20-1.46 (m, 28 H, CH_2), 1.39 (s, 2 H, OH), 1.46-1.65 (m, 4 H, CH_2), 1.65-1.82 (m, 4 H, CH_2), 2.87 (t, *J* = 7.3 Hz, 4 H, S-CH_2), 3.64 (t, *J* = 6.5 Hz, 4 H, O-CH_2).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 63.0, 38.8, 32.7, 29.5, 29.4, 29.1, 28.8, 28.5, 25.7. Signals: expected, 11; observed, 9.

HRMS (ESI): *m*/*z* [M + Na]+ calcd for $C_{22}H_{46}NaO_2S_3$: 461.2558; found: 461.2556.

Bis(10-carboxydecyl) trisulfide (5c)

Chromatography ($CHCl_3$–MeOH, 25:1); yield: 92%; white solid mp 79–81 °C

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.24-1.50 (m, 24 H, CH_2), 1.54-1.84 (m, 8 H, CH_2), 2.36 (t, *J* = 7.3 Hz, 4 H, CH_2COO), 2.88 (t, *J* = 7.3 Hz, 4 H, S-CH_2), 8.90 (brs, 2 H, COOH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 180.2, 38.8, 34.0, 29.3, 29.3, 29.1, 29.1, 29.0, 28.8, 28.4, 24.6. Signals: expected, 11; observed, 11.

HRMS (ESI): *m*/*z* [M + Na]+ calcd for $C_{22}H_{42}NaO_4S_3$: 489.2143; found: 489.2151.

Bis(2-hydroxyethyl) trisulfide (5d)

Chromatography ($CHCl_3$–MeOH, 25:1); yield: 81%; colorless oil. (Lit.[15, 28])

^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.16 (s, 2 H, OH), 3.09 (t, *J* = 5.7 Hz, 4 H, S-CH_2), 3.99 (t, *J* = 5.7 Hz, 4 H, O-CH_2).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 59.5, 41.7. Signals: expected, 2; observed, 2.

HRMS (ESI): *m*/*z* [M + Na]+ calcd for $C_4H_{10}NaO_2S_3$: 208.9741; found: 208.9736.

Bis[(*R*)-2-(*tert*-butoxycarbonylamino)-2-(ethoxycarbonyl)ethyl] trisulfide (5e)

Chromatography (CH_2Cl_2–ethyl acetate, 25:1); yield: 92%; white solid mp 74–77 °C

^{1}H NMR (200 MHz, CDCl3): δ = 1.30 (t, *J* = 7.1 Hz, 6 H, $COOCH_2CH_3$), 1.46 (s, 18 H, Boc), 3.37 (d, *J* = 4.8 Hz, 4 H, SCH_2), 4.23 (q, *J* = 7.1 Hz, 4 H, $COOCH_2$), 4.56-4.72 (m, 2 H, CH), 5.44 (d, *J* = 7.8 Hz, 2 H, BocNH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 170.3, 155.0, 80.2, 61.9, 52.9, 41.1, 28.3, 14.1. Signals: expected, 8; observed, 8.

HRMS (ESI): *m*/*z* [M + Na]+ calcd for $C_{20}H_{36}N_2NaO_8S_3$: 551.1531; found: 551.1527.

Bis(p-tolyl) trisulfide (5f)

Chromatography (CH_2Cl_2–petroleum ether, 1:2); yield: 87%; bright yellow solid mp 76–77 °C (Lit.[5a] 78-79 °C)

^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.36 (s, 6 H, CH_3), 7.12 (d, *J* = 7.9 Hz, 4 H, Ar), 7.45 (d, *J* = 7.9 Hz, 4 H, Ar).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.6, 131.0, 129.8, 128.5, 21.2. Signals: expected, 5; observed, 5.

HRMS (ESI): *m*/*z* [M + Na]+ calcd for $C_{14}H_{14}NaS_3$: 301.0155; found: 301.0160.

Symmetrical trisulfides 5 from 4a-f; General Procedure (Method B)

A solid thioacetamide (83 mg, 1.1 mmol) was added to a soln of one of **4a-f** (2.0 mmol) and Et_3N (0.293 mL, 2.1 mmol) in CH_2Cl_2 (20 mL) at 0 °C under air atmosphere. The mixture was stirred at 0 °C for 30 min, and evaporated under vacuum. Then Et_2O (100 mL) was added and mixture was washed with H_2O (50 mL), dried ($MgSO_4$), filtered, and evaporated under vacuum. The residue was purified by column chromatography; this gave **5a-f**. The yields are reported in Table 2.

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References

(1) (a) Higuchi, O.; Tateshita, K.; Nishimura, H. *J. Agric. Food Chem*. **2003**, *51*, 7208. (b) Schregen, L.; Diriack, P.; Van Wassehove, F.; Schamp, N. *J. Agric. Food Chem*. **1976**, *24*, 336.

(2) Nicolaou, K. C.; Hummel, C. W.; Nakada, M.; Shibayama, K.; Pitsinos, E. N.; Saimoto, H.; Mizuno, Y.; Baldenius, K.-U.; Smith, A. L. *J. Am. Chem. Soc*. **1993**, *115*, 7625.

(3) Kumar, R. A.; Ikemoto, N.; Patel, D. J. *J. Mol. Biol*. **1997**, *265*,173.

(4) Schöberl, A.; Wagner, A. in Houben-Weyl, Modern der Organischen Chemie 4th. Edn., Müller, E. Ed., vol. 9, Georg Thieme Verlag, Stuttgart, 1955, p. 87-90.

(5) (a) Zysman-Colman, E.; Harpp, D. N. *J. Org. Chem*. **2003**, *68*, 2487. (b) Clayton, J. O.; Etzler, D. H. *J. Chem. Soc.* **1974**, *69*, 974.

(6) Fuson, R. C.; Price, Ch. C.; Burness, D. M.; Foster, R. E.; Hatchard, W. R.; Lipscomb, R. D. *J. Org. Chem*. **1946**, *11*, 487.

(7) Sato, R.; Saito, S.; Chiba, H.; Goto, T.; Saito, M. *Chem. Lett*. **1986**, 349.

(8) Schimmelschmidt, K.; Hoffmann, H.; Mundlos, E. *Chem. Ber.* **1963**, *96*, 38.

(9) Buckman, J. D.; Field, L. *J. Org. Chem.* **1967**, *32*, 2.

(10) Mott, A. W.; Barany, G. *Synthesis* **1984**, 657.

(11) Hayashi, S.; Furukawa, M.; Yamamoto, J.; Hamamura, K. *Chem. Pharm. Bull.* **1967**, *15*, 1310.

(12) Capozzi, G.; Capperucci, A.; Degl'Innocenti, A.; Del Duce, R.; Menichetti, S. *Tetrahedron Lett*. **1989**, *30*, 2991.

(13) (a) Arisawa, M.; Tanaka, K.; Yamaguchi, M. *Tetrahedron Lett*. **2005**, *46*, 4797. (b) Hou, Y.; Abu-Yousef, I. A.; Doung, Y.; Harpp, D. N. *Tetrahedron Lett*. **2001**, *42*, 8607.

(14) Harpp, D. N.; Granata, A. *Tetrahedron Lett*. **1976**, 3001.

(15) Wu, Z.; Back, T. G.; Ahmad, R.; Yamdagni, R.; Amstrong, D. A. *J. Phys. Chem.* **1982**, *86*, 4417.

(16) An, H.; Zhu, J.; Wang, X.; Xu, X. *Bioorg. Med. Chem. Lett*. **2006**, *16*, 4826.

(17) Nakabayashi, T.; Tsurugi, J. *J. Org. Chem*. **1961**, *26*, 2482.

(18) Böhme, H.; Van Ham, G. *Justus Liebigs Ann. Chem*. **1958**, *617*, 62

(19) Harpp, D. N.; Derbesy, G. *Tetrahedron Lett*. **1994**, *35*, 5381.

(20) Kresze, G.; Patzscheke, J. *Chem. Ber*. **1960**, *93*, 380.

(21) Antoniow, S.; Witt, D. *Synthesis*, **2007,** 363.

(22) Kowalczyk, J.; Barski, P; Witt, D.; Grzybowski, B. A. *Langmuir*, **2007**, *23*, 2318.

(23) Szymelfejnik, M.; Demkowicz, S.; Rachon, J.; Witt, D. *Synthesis*, **2007,** 3528.

(24) Demkowicz, S.; Rachon, J.; Witt, D. *Synthesis*, **2008,** 2033.

(25) Pappo, D.; Kashman, Y. *Org. Lett.* **2006**, *8*, 1177.

(26) Edmundson, R. S. *Tetrahedron*, **1965**, *21*, 2379.

(27) Carmona, E.; Contreras, L.; Sanches, L. J.; Gutierrez-Puebla, E.; Monge, A. J. Chem. Soc., Dalton Trans. **1989**; 2003.

(28) Kohama, Y.; Iida, K.; Semba, T.; Mimura, T.; Inada, A. *Chem. Pharm. Bull*. **1992**, *40*, 2210.

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