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Methylenetriimidosulfate $H_2CS(NtBu)_3^{2-}$—The First Dianionic Sulfur(VI) Ylide**

Bernhard Walfort and Dietmar Stalke*

Isoelectronic replacement of the oxygen atoms in simple p-block element oxoanions by an NR imido group is currently a flourishing area of main group chemistry.[1] These new species are soluble in nonpolar organic solvents because they form contact-ion pairs, whose periphery consists of lipophilic substituents. In contrast, the simple oxoanions form infinite solid-state lattices as a result of the multiple oxygen – metal cation contacts. We were particularly interested in the polyimidosulfur anions because of the rich redox chemistry.[2]

Triimidosulfite $S(NR)_3^{2-}$,[3] which is analoguous to sulfite SO_3^{2-}, can be radically oxidized to $S(NR)_3$ (Scheme 1).[4] The cap-shaped $S(NR)_3^{2-}$ ion is the first tripodal coordinating dianion.[5] Tetraimidosulfate $S(NR)_4^{2-}$, which is analogous to sulfate SO_4^{2-}, [6] gives soluble monomeric metal complexes.[7]

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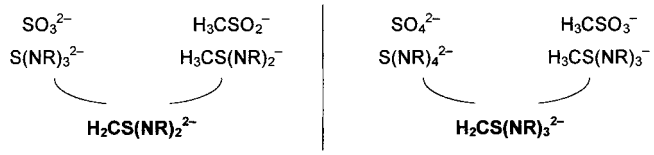
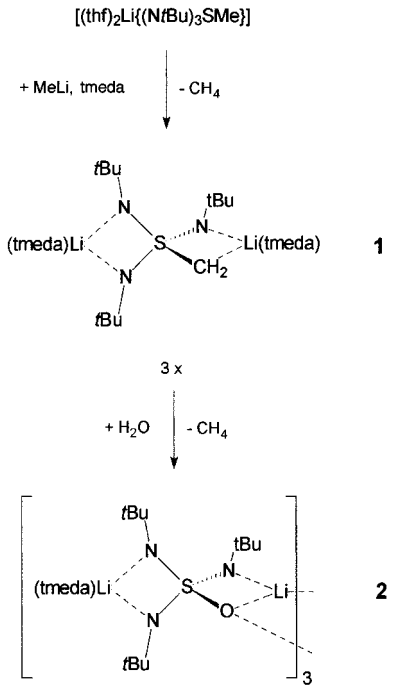


Scheme 1. Isoelectronic C and N analogues of SO_3^{2-} and SO_4^{2-}.

We now focus on isoelectronic replacement of the oxygen atoms in the sulfur oxoanions and the imido groups in polyimidosulfur anions by a R_2C^- group. Sulfur compounds containing a metalated α-carbon atom are well established.[8] Sulfur ylides, which like Wittig ylides can be employed for C–C coupling reactions, are utilized most frequently in synthesis.[9] Sulfoximines are also used in asymmetric C–C coupling reactions.[10] The C_α-deprotonation of the S-bonded substituent in diimidosulfinates $R_2(H)CS(NR)_2^-$[11] yields the dianionic methylenediimidosulfites $R_2CS(NR)_2^{2-}$ (Scheme 1), the carba/imido analogues of SO_3^{2-}.[12] Herein we present the alkylenetriimidosulfate $[(tmeda)_2Li_2\{H_2CS(NtBu)_3\}]$ (**1**) (tmeda = $Me_2NCH_2CH_2NMe_2$), the first carba/imido analogue of SO_4^{2-}.

Compound **1** can be synthesized readily starting from lithium *S*-methyltri(*tert*-butyl)triimidosulfonate $H_3CS(NtBu)_3^-$ by deprotonation of the *S*-methyl group with methyllithium in high yields (Scheme 2). The addition of two equivalents of MeLi to *S*-alkyltri(*tert*-butyl)triimidosulfonic acid $RS(NtBu)_2NHtBu$ provides a second route to **1**.[2b, 13] $[(tmeda)_2Li_2\{H_2CS(NtBu)_3\}]$ (**1**) crystallizes in the presence of the donor base tmeda.

Compound **1** is, like $[(thf)_2Li_2\{(NtBu)_4S\}]$[6] and $[\{Li_2[(NtBu)_3S]\}_2]$,[3] air- and moisture-sensitive. Reaction of **1** with one equivalent of water gives the trimeric triimidosulfate $[\{(tmeda)Li_2[OS(NtBu)_3]\}_3]$ (**2**), indicating that the methylene substituent is hydrolyzed to form methane preferentially to the hydrolysis of an imido substituent to give an amine.



Scheme 2. Synthesis of **1** and **2**.

The crystal structure of **1** (Figure 1) consists of separated contact-ion pairs.[14] The sulfur atom is surrounded in a distorted tetrahedral fashion by three imido groups and one

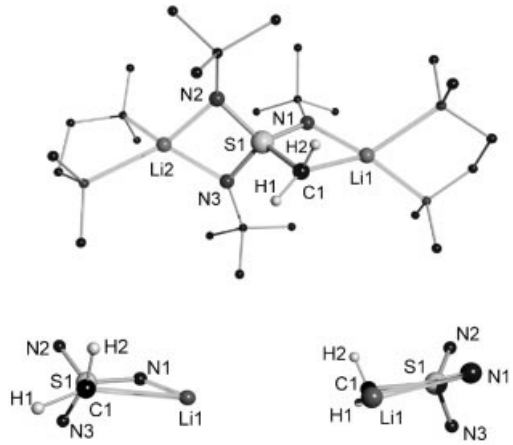


Figure 1. Top: Crystal structure of **1**. Bottom left: Projection along the S1–C1 bond. Bottom right: Projection along the Li1–C1 bond. Selected bond lengths [pm] and angles [°]: S1-C1 172.5(2), S1-N1 160.50(19), S1-N2 159.0(2), S1-N3 161.4(2), C1-H1 101(3), C1-H2 85(3), C1-Li1 213.2(5), N1-Li1 195.9(5), N2-Li2 195.4(4), N3-Li2 199.8(4); C1-S1-N1 97.66(12), N2-S1-N3 96.05(10), N1-S1-N2 117.32(11), C1-S1-N3 120.47(13), C1-S1-N2 111.64(14), N1-S1-N3 115.08(11).

methylene moiety (Figure 1, top). The two lithium atoms bridge two opposite edges of the SN_3C tetrahedron, narrowing the related S-N-N (N2-S1-N3 96.05(10)°) and S-N-C angles (C1-S1-N1 97.66(12)° in contrast to the angle between the nonbridged coordinating atoms of av 116.0(2)°). The average S–N and Li–N bond lengths of 160.3 and 197.0 pm, respectively, are similar to those found in $[(thf)_4Li_2\{S(NtBu)_4\}]$.[6] The most remarkable structural feature involves the bonding and orientation of the CH_2 group to the central sulfur atom. The S1–C1 bond length in **1** is only 172.5(3) pm and thus 6.7 pm shorter than the average value of 179.2 pm in *S*-methyltri(*tert*-butyl)triimidosulfonate $H_3CS(NtBu)_3^-$.[13] However, this bond shortening upon deprotonation should not be attributed to S=C bonding in the sulfur ylenic mesomeric form. Although this distance is considerably shorter than in most α-sulfonyl carbanions,[15] in the 2,2-diphenyl-1-(phenylsulfonyl)cyclopropyllithium complex $[\{(dme)Li[Ph_2C_3H_2SO_2(Ph)]\}_2]$ (dme = 1,2-dimethoxyethane) the corresponding distance is only 167.6(7) pm.[15d] Despite this short distance the lithiated carbon atom resides in a tetrahedral environment. The S–C bond length in **1** is similar to the observed S–C(sp) bond length of 171.8(3) pm in $[(thf)_2Li\{(NtBu)_3SC{\equiv}CPh\}]$.[13] The metalated C1 center in **1** is only about 26 pm above the H1/H2/Li1 and H1/S1/Li1 plane suggesting that hybridization state of C1 lies between sp^3 and sp^2. The shortening of the S–C bond is attributed to a radius reduction on the change in hybridization $sp^3 \rightarrow sp^2$, electrostatic $S^{\delta+}-C^{\delta-}$ attraction and hyperconjugation, rather than to a d-orbital contribution.[16] It is remarkable that the freely refined hydrogen atoms of the methylene group are not located along the bisector of the S1-C1-L1 angle. H2 is tilted towards Li1 causing a relatively close Li1 ··· H2 contact of 223(3) pm (Figure 1, bottom).

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Isoelectronic replacement of the methylene group in **1** by an oxygen atom gives the trimer **2**.[14] The triimidosulfate dianion is (*N*,*N*′),(*N*,*O*)-dichelated to two lithium cations on opposite edges of the OSN_3 tetrahedron (Figure 2, left). While the outer *N*,*N*′-chelated lithium cation is tetrahedrally coordinated by the additional chelating donor base tmeda, the *N*,*O*-chelated lithium atom is trigonal planar coordinated providing the second intramolecular Li–O link around the threefold axis (Figure 2, right). Hence the trimer consists of a planar central Li_3O_3 six-membered ring with three annelated planar LiOSN four-membered rings. The three peripheral LiN_2S rings are arranged orthogonal relative to these four fused rings.

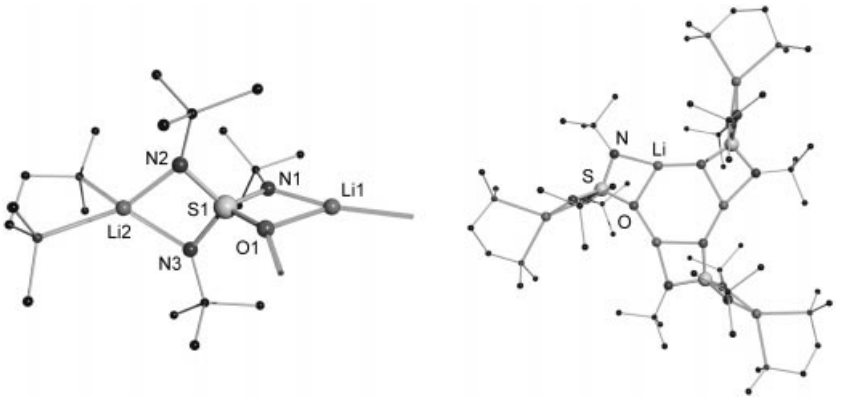
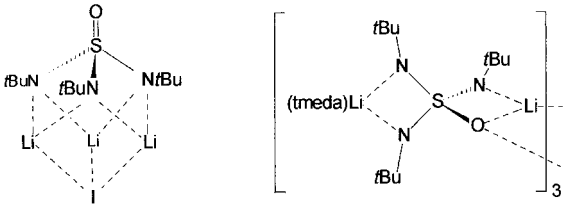


Figure 2. Left: Asymmetric unit of **2**. Right: Structure of the trimer with the threefold axis orthogonal to the paper plane in the centre of the Li_3O_3 six-membered ring. Selected bond lengths [pm] and angles [°]: S1-O1 151.73(19), S1-N1 157.5(3), S1-N2 156.8(6), S1-N3 153.8(6), O1-Li1 181.3(6), O1-Li1A 196.5(6), N1-Li1A 190.4(6), N2-Li2 187.8(14), N3-Li2 205.5(12); O1-S1-N1 97.09(12), N2-S1-N3 98.57(15), N1-S1-N2 118.9(4), O1-S1-N3 111.8(3), O1-S1-N2 115.1(3), N1-S1-N3 116.3(4), Li1A-O1-Li1 117.2(3), O1-Li1-O1A 122.8(3).

The S1–O1 bond with the lithium-coordinated O atom in **2** of 151.73(19) pm is considerably longer than the terminal S–O bond in the only other known triimidosulfate dianion $OS(NtBu)_3^{2-}$ (145.5(5) pm).[4] This difference is caused by the different coordination mode in the two compounds. In **2** the electron density has to be shared between the two lithium cations and the electropositive sulfur atom (Scheme 3).



Scheme 3. Different coordination modes of the two known triimidosulfate dianions

In the 36-atom clusters of $[\{Li_2[OS(NR)(NR')]\}_6]$, which contain a pyramidal diimidosulfite dianion, the six oxygen atoms are each coordinated by three lithium atoms, which leads to an elongation of the average S–O bond to 154.6(13) (R = *t*Bu, R′ = $SiMe_3$) and to 158.7(7) pm (R = R′ = *t*Bu).[17] The metal diimidosulfates $O_2S(NtBu)_2^{2-}$ tend to form clusters as well because of two metal-bridging oxygen atoms. The lithium diimidosulfate comprises an octamer,[18] while the mixed-metal Li/Mg cluster contains twelve dianions, as well as eight lithium and two magnesium cations.[19] The mixed-metal Li/Al compounds form polymeric strands in the solid state.[20]

In conclusion, both the elongation of the S–O and shortening of the S–C bond can be attributed to electrostatics. We favor ylidic $S^+–C^-$ rather than ylenic S=C bonding.[21] This interpretation and the preferred hydrolysis of the methylene group over the imido group in the reaction of **1** to give **2** suggests that **1** could be employed as a methylene transfer reagent similar to the Wittig phosphonium ylides.

Experimental Section

All manipulations were performed under an inert gas atmosphere of dry N_2 with Schlenk techniques or in an argon glovebox. All solvents were dried over Na/K alloy and distilled prior to use. ^1H, ^7Li and ^{13}C NMR spectra were recorded in C_6D_6 (internal standards C_6HD_5: $\delta = 7.15$ (^1H), C_6D_6: $\delta = 128.0$ (^{13}C) using a Bruker AMX 400 spectrometer. Elemental analyses were performed by the Microanalytisches Labor der Universität Würzburg.

Synthesis of $[(tmeda)_2Li_2\{H_2CS(NtBu)_3\}]$ (**1**): Methyllithium (10.14 mmol, 3.4 mL of a 3 M solution) was added slowly at −78 °C to a solution of $[(thf)_2Li_2\{(NtBu)_3SMe\}_2]$ (5.07 mmol, 3.0 g), prepared as described in ref. [6], in THF (20 mL) and stirred for 1 h. Instantaneous formation of methane gas was observed. The solution was then stirred for two hours at room temperature. Subsequently, THF was removed in vacuum and the white precipitate was redissolved in warm hexane and tmeda. Storage of the solution at −36 °C for three days afforded colorless crystals which were suitable for single-crystal X-ray structure analysis (yield 2.6 g, 78%). ^1H NMR (400.13 MHz, C_6D_6): $\delta = 1.58$ (2H; SCH_2), 1.73 (s, 9H; $NC(CH_3)_3$), 1.77 (s, 18H; $NC(CH_3)_3$), 1.89 (s, 8H; NCH_2CH_2N), 2.13 (s, 24H; $N(CH_3)_2$); ^{13}C NMR (100 MHz, C_6D_6): $\delta = 34.61$ (SCH_2), 34.85 ($NC(CH_3)_3$), 35.03 ($NC(CH_3)_3$), 46.55 (NCH_2CH_2N), 51.65 ($NC(CH_3)_3$), 52.17 ($NC(CH_3)_3$), 57.26 (s, 24H; $N(CH_3)_2$); ^7Li NMR (155.5 MHz, ext. sat. LiCl solution): $\delta = 0.85$, 1.24; elemental analysis (%): calcd: C 59.37, H 12.16, N 19.39, S 6.34: found: C 57.43, H 10.24, N 20.45, S 7.26.

Synthesis of $[\{(tmeda)Li_2[OS(NtBu)_3]\}_3]$ (**2**): H_2O (1.48 mmol) in tmeda (10 mL) was slowly added at −10 °C to a solution of **1** (1.48 mmol, 0.75 g) in hexane (20 mL). The reaction mixture was stirred for 1 h at −10 °C and then 2 h at room temperature. The solvent was removed in vacuum and the white precipitate was redissolved in warm hexane and tmeda. Storage of the solution at −36 °C for several days afforded colorless crystals which were for single-crystal X-ray structure analysis (yield 0.3 g, 51%). ^1H NMR (400.13 MHz, C_6D_6): $\delta = 1.47$ (s, 9H; $NC(CH_3)_3$), 1.49 (s, 18H; $NC(CH_3)_3$), 1.61 (s, 8H; NCH_2CH_2N), 2.05 (s, 24H; $N(CH_3)_2$); ^{13}C NMR (100 MHz, C_6D_6): $\delta = 33.39$ ($NC(CH_3)_3$), 33.63 ($NC(CH_3)_3$), 34.62 (NCH_2CH_2N), 46.25 ($N(CH_3)_2$), 51.70 ($NC(CH_3)_3$), 51.95 ($NC(CH_3)_3$); ^7Li NMR (155.5 MHz, ext. sat. LiCl solution): $\delta = 0.5$, 1.79; elemental analysis (%):calcd: C 55.22, H 11.07, N 17.89, S 8.19; found: C 52.11, H 12.32, N 19.28, S 7.78.

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[14] Crystal structure data for **1** and **2**: The data were collected from shock-cooled crystals on an BRUKER SMART-APEX CCD diffractometer (graphite-monochromated $Mo_{K\alpha}$ radiation, $\lambda = 71.073$ pm) equipped with a low-temperature device at 193(2) K.[22] The structures were solved by direct methods (SHELXS-97)[23] and refined by full-matrix least-squares methods against F^2 (SHELXL-97).[24] R values defined as $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$, $wR2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{0.5}$, $w = [\sigma^2(F_o^2) + (g_1P)^2 + g_2P]^{-1}$, $P = 1/3[\max(F_o^2,0) + 2F_c^2]$. **1**: $C_{25}H_{61}Li_2N_7S$, $M_r = 505.75$, orthorhombic, space group *Pbca*, $a = 1996.67(13)$, $b = 1649.92(10)$, $c = 2027.39(14)$ pm, $V = 6.6789(8)$ nm^3, $Z = 8$, $\rho_{calcd} = 1.006$ Mg m^{-3}, $\mu = 0.120$ mm^{-1}, $F(000) = 2256$, 26858 reflections measured, 4730 unique, $R(\text{int}) = 0.0931$, $wR2(\text{all data}) = 0.1880$, $R1(I > 2\sigma(I)) = 0.0657$, $g_1 = 0.1225$, $g_2 = 1.6000$ for 341 parameters and no restraints. **2**: $C_{18}H_{43}Li_2N_5OS$, $M_r = 391.51$, hexagonal, space group $P6_3$, $a = b = 1768.91(8)$, $c = 1506.06(10)$ pm, $V = 4.0812(4)$ nm^3, $Z = 6$, $\rho_{calcd} = 0.956$ Mg m^{-3}, $\mu = 0.132$ mm^{-1}, $F(000) = 1296$, 16134 reflections measured, 3887 unique, $R(\text{int}) = 0.0647$, $wR2(\text{all data}) = 0.1679$, $R1(I > 2\sigma(I)) = 0.0627$, $g_1 = 0.0974$, $g_2 = 0.0$ for 337 parameters and 289 restraints and a Flack x parameter of 0.2(2).[25] The hydrogen atoms at the methylene atom C1 in **1** were located by difference Fourier syntheses and refined freely. All other hydrogen atoms of the molecule were refined by using a riding model. Compound **2** crystallized in the noncentrosymmetric space group $P6_3$. An additional mirror plane in the O_3Li_3 ring plane to give the higher symmetric space group $P6_3/m$ is precluded by the coordinated tmeda molecules and the N-bonded *tert*-butyl groups. As the chirality is induced only in the periphery strictly spoken the molecule is not planar chiral.[26] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos CCDC-164904 (**1**) and CCDC-164905 (**2**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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Total Synthesis of Apoptolidin: Part 1. Retrosynthetic Analysis and Construction of Building Blocks**

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From the many macrolide type structures recently isolated from nature, that of apoptolidin (**1**, Scheme 1),[1] isolated from *Nocardiopsis* sp., stands out. Its distinction as a synthetic

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Supporting information for this article (selected physical properties of compounds **2**, **3**, **4**, **51**, and **69**) is available on the WWW under http://www.angewandte.com or from the author.