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Unexpected reactivity of 3-ethylsulfonyl-1,2,4-triazines with $\mathrm{B_{12}H_{11}SH}\rceil^{2-}$: first examples of the synthesis of boron-centered *as*-triazines and thioesters of ethyl sulfinic acid

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The reaction of 3-ethylsulfonyl-5-methylamino-6-methylcarboxamido-1,2,4-triazine 1 with $\mathrm{B_{12}H_{11}SH}\rceil^{2-}$ yields the boron-containing derivatives of 1,2,4-triazine 3. The interaction of 5,7-dimethyl-5,6,7,8-tetrahydropyrimido[4,5-*e*][1,2,4]triazine-6,8-dione 2 with mercaptoborane $\mathrm{B_{12}H_{11}SH}\rceil^{2-}$ gives boron-containing thiosulfinate 4 and bis(heteryl) ether 5.

Amino derivatives of 6-azalumazine may be produced by the nucleophilic substitution of the 3-alkylthio group in 5,6,7,8-tetrahydropyrimido[4,5-*e*][1,2,4]triazine-6,8-diones.[1] Alkylsulfonic groups possess a much higher nucleofugity than alkylthio groups. Thus, it was found[2–4] that the 3-alkylsulfonic group in 5,7-dimethyl-5,6,7,8-tetrahydropyrimido[4,5-*e*]-[1,2,4]triazine-6,8-dione may be easily substituted in reactions with amines, water, sodium sulfide, sodium azide and various C-nucleophiles.

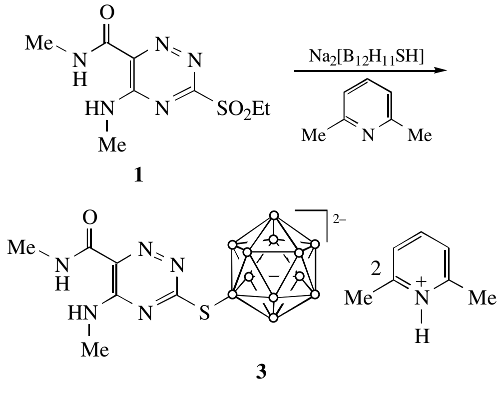
We studied the nucleophilic substitution of alkylsulfonic derivatives of *as*-triazine with the mercaptoborane $\mathrm{B_{12}H_{11}SH}\rceil^{2-}$ as a nucleophile, which can be alkylated and acylated to produce sulfonium ions or thio esters.[5]

3-Ethylsulfonyl-5-methylamino-6-methylcarboxamido-1,2,4-triazine **1** and 3-ethylsulfonyl-5,7-dimethyl-5,6,7,8-tetrahydropyrimido[4,5-*e*][1,2,4]triazine-6,8-dione **2** (produced by the oxidation of corresponding alkylthio derivatives as described earlier[2,3]) were used as starting heterylsulfones for reactions with $\mathrm{B_{12}H_{11}SH}\rceil^{2-}$.

We found that sulfone **1** reacted with $\mathrm{B_{12}H_{11}SH}\rceil^{2-}$ at room temperature in the presence of lutidine to form the boron-containing derivatives of 1,2,4-triazine **3** (Scheme 1).[†,‡]

The ^{1}H NMR spectrum of compound **3** contains proton signals of 5-MeNH and 6-MeNH substutients of *s*-triazine and the signals of protons of two molecules of lutidine. The negative-ion fast atom bombardment (FAB) mass spectrum shows an ion at *m/z* 339, which corresponds to the boron-containing molecular anion of compound **3**. In the positive-ion FAB spectrum, an ion at *m/z* 108 corresponding to the protonated lutidine ($C_7H_{10}N$) is observed.

We obtained unexpected products from the reaction of sulfone **2** with $\mathrm{Na_2[B_{12}H_{11}SH]}$ under similar conditions (Scheme 2).[†,‡]



○ = B or BH

Scheme 1

Instead of a nucleophilic attack on the 3-carbon atom of heterocyclic compound **2** with the substitution of the alkylsulfonyl group, the boron-bonded thiol attacked the sulfur atom of the sulfone. As a result, in this case, unknown compounds **4** and **5** were obtained.

The ^{1}H NMR spectrum of **4** contains proton signals of the Et group and of lutidine with the expected ratio 1:2 between these groups.[‡]

X-ray structure analysis showed that compound **4** is the crystalline hydrate of the salt of the doubly charged anion of

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[†] *Reaction of sulfone* **1** *with* $\mathrm{Na_2[B_{12}H_{11}SH]}$. 0.078 g (0.3 mmol) of sulfone **1** was stirred with 0.095 g (0.43 mmol) of $\mathrm{Na_2[B_{12}H_{11}SH]}$ in 2 ml of acetonitrile in the presence of 0.05 ml of lutidine for 3 h at room temperature. The reaction mixture was filtered, and the filtrate was evaporated *in vacuo*. The residue was treated with 2 ml of water, and **3** was obtained as a solid. The product was recrystallised from water; yield 0.053 g (33%), mp 148–150 °C.

Reaction of sulfone **2** *with* $\mathrm{Na_2[B_{12}H_{11}SH]}$. 0.470 g (1.60 mmol) of sulfone **2**, 0.360 g (1.63 mmol) of $\mathrm{Na_2[B_{12}H_{11}SH]}$ and 0.2 ml of lutidine were stirred in 10 ml of acetonitrile for 1 h at room temperature. Crystals of di(5,7-dimethylpyrimido[4,5-*e*][1,2,4]triazin-3-yl)ether **5** were filtered off. Product **5** precipitated from dimethyl sulfoxide with ethanol with a yield of 0.20 g (30%), mp > 250 °C.

The mother liquor was evaporated *in vacuo*, the residue was treated with 2 ml of ethanol, filtered, and crystallised from 30% water/ethanol. Compound **4** [0.250 g (32%) yield] was obtained, mp 170–171 °C.

0.066 g (0.16 mmol) of product **5** was suspended in 8 ml of water, 0.2 ml trifluoroacetic acid was added, the mixture was stirred for 3–5 min and filtered. The filtrate was evaporated *in vacuo*, the residue was treated with 1 ml of water and filtered to yield 0.01 g (29%) of 3-hydroxy-5,7-dimethyl-5,6,7,8-tetrahydropyrimido[4,5-*e*][1,2,4]triazine-6,8-dione **6**, mp > 250 °C.

[‡] ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX 200 spectrometer. Chemical shifts were measured relative to DMSO as an internal standard.

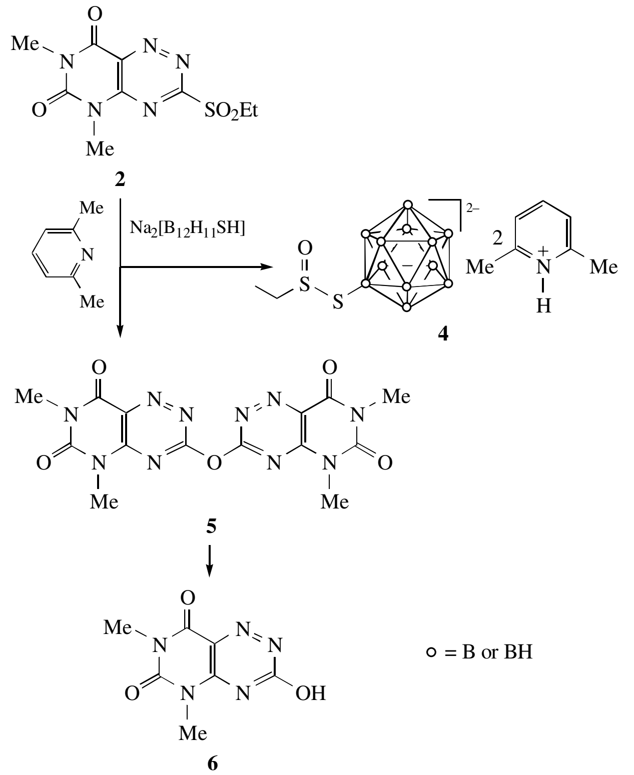
Mass spectra were measured on a Finnigan MAT 8200 double-focusing mass spectrometer. Electron impact (EI) ionization conditions: electron energy of 70 eV and ion source temperature of 200 °C. Fast atom bombardment (FAB) mass spectra were recorded using a Xe atom gun (beam energy of 8 keV) and 3-nitrobenzyl alcohol (NBA) as the matrix.

For **3**: ^{1}H NMR ([$^2H_6$]DMSO) δ: 2.66 (s, 12H, 4Me lutidine), 2.71 (d, 3H, NMe, *J* 4.9 Hz), 3.01 (d, 3H, NMe, *J* 5.4 Hz), 7.69 (d, 4H, 2×3-H and 2×5-H lutidine, *J* 7.8 Hz), 8.32 (t, 2H, 2×4-H lutidine, *J* 7.8 Hz), 9.11 (q, 1H, NH, *J* 5.4 Hz), 10.15 (q, 1H, NH, *J* 4.9 Hz). ^{13}C NMR ([$^2H_6$]DMSO) δ: 20.11 (2Me lutidine), 26.78 (NMe), 29.23 (NHMe), 125.52 (2×C^3,C^5 lutidine), 131.65 (C triazine), 146.58 (2×C^4 lutidine), 152.32 (C triazine), 153.83 (2×C^2,C^6 lutidine), 162.80, 172.28 (C triazine).

For **4**: ^{1}H NMR ([$^2H_6$]DMSO) δ: 1.14 (t, 3H, Me, *J* 7.5 Hz), 2.67 (s, 6H, 2Me lutidine), 2.79 (q, 2H, CH_2, *J* 7.5 Hz), 7.70 (d, 4H, 2×3-H and 2×5-H lutidine, *J* 7.8 Hz), 8.34 (t, 2H, 2×4-H lutidine, *J* 7.8 Hz). ^{13}C NMR ([$^2H_6$]DMSO) δ: 8.36 (Me), 20.16 (4Me lutidine), 52.71 (CH_2), 125.56 (2×C^3,C^5 lutidine), 146.63 (2×C^4 lutidine), 153.80 (2×C^2,C^6 lutidine).

For **5**: ^{1}H NMR ([$^2H_6$]DMSO) δ: 3.20 (s, 3H, NMe), 3.26 (s, 3H, NMe). ^{13}C NMR ([$^2H_6$]DMSO) δ: 27.79 (Me), 28.32 (Me), 123.21, 152.02, 152.82, 160.34, 165.82 (C_{hetaryl}).

For **6**: ^{13}C NMR ([$^2H_6$]DMSO) δ: 29.02 (Me), 29.47 (Me), 125.14, 151.33, 154.40, 155.24, 157.91 (C_{heteryl}).



Scheme 2

the boron-containing thioester of ethylsulfinic acid with two molecules of protonated lutidine {(2,6-$Me_2C_5H_3NH)_2$-$[B_{12}H_{11}SS(O)Et]\cdot H_2O$, Figure 1}.[§] The thiosulfinate group of the crystals of **4** is an irregular pyramide with the sulfoxide S-atom on top and the sulfide S-atom, oxygen and CH_2 group forming the base of the pyramide. The bond lengths are: S–O, 148.6 pm; S–S, 208.8 pm; B–S, 189.8 pm; S–C, 181.2 pm.

In the ^{1}H NMR spectrum of compound **5** only signals of the N–Me groups of the pyrimidine part of the molecule are present.[‡] The ^{13}C NMR spectrum of **5** contains seven signals of the pyrimidotriazine fragment (5 C-atoms of the pyrimidotriazine ring and 2 C-atoms of N–Me groups).[‡]

The molecular formula $C_{14}H_{12}N_{10}O_5$ of product **5** was confirmed by high resolution mass spectrometry (HRMS) (theor. 400.09921, confirmed ±5 ppm). Investigation of the cleavage paths and products by the DADI (Direct Analysis of Daughter Ions) technique showed that the ions at *m/z* 385 (M – Me), 372 ($C_{14}H_{12}N_8O_5$, exp. 372.09273, theor. 372.09307, Δ 0.9 ppm, M – N_2) are formed directly from the molecular ion at *m/z* 400. Using precursor ion analysis, we found that the ion at *m/z* 208 originates from the ions with *m/z* 220, 223, 287, 372 and 400. The proof of *m/z* 208 ($C_7H_6N_5O_3$, exp. 208.04616, theor. 208.04706, Δ 0.9 ppm) originating from the molecular ion (*m/z* 400) by this scanning technique is especially important since this could not be confirmed by DADI due to the low intensity of this ion.

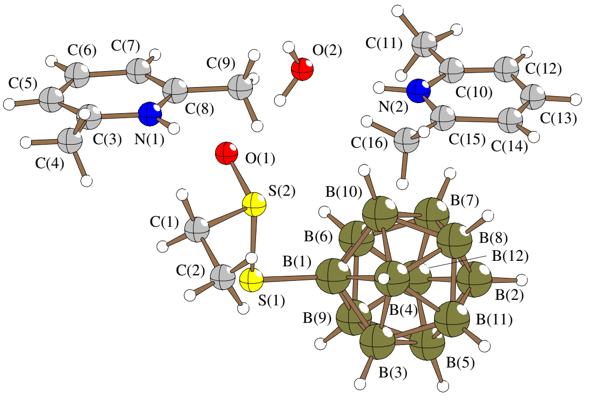
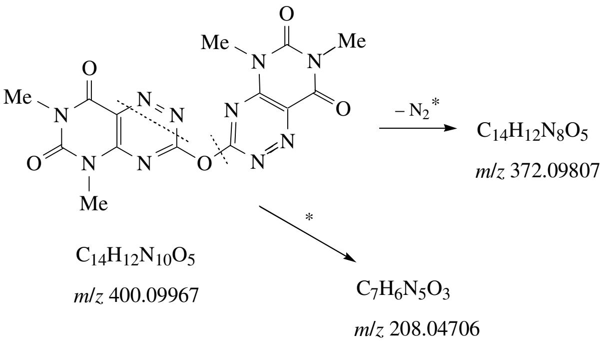


Figure 1 Molecular structure of compound **4**. Selected bond lengths (Å): C(1)–C(2) 1.53(1), S(1)–B(1) 1.898(8), S(1)–S(2) 2.088(3), S(2)–C(1) 1.81(1), S(2)–O(1) 1.486(5). Selected bond angles (°): B(1)–S(1)–S(2) 96.0(3), O(1)–S(2)–C(1) 105.0(5), O(1)–S(2)–S(1) 108.4(3), C(1)–S(2)–S(1) 96.8(3), C(2)–C(1)–S(2) 110.5(8).



Scheme 3

During crystallization of compound **5** from aqueous acid solutions, we isolated 3-hydroxy derivative **6**.[1] Probably, the formation of **6** is connected with easy hydrolysis of **5** under these conditions.

Thus, depending on the nature of the hetarylic substituent, two different reactivities of sulfonic derivatives with $B_{12}H_{11}SH^{2-}$ may occur:

(1) a nucleophilic attack of $B_{12}H_{11}SH^{2-}$ on the C-3 atom of the triazine ring of sulfone **1**, cleaving off ethylsulfonic acid and leading to formation of undecahydrododecaboranylthio-5-methylamino-6-methylcarboxamido-1,2,4-triazine **3**;

(2) an attack of $B_{12}H_{11}SH^{2-}$ on the S-atom of the 3-sulfonic group of pyrimidotriazine **2** leading to the formation of a boron-containing thioester of ethylsulfinic acid **4** and bis(heteryl) ether **5**.

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[§] *Crystal data for* **4**: at 173(2) K, a crystal of $C_{16}H_{36}N_2B_{12}OS_2\cdot H_2O$ (0.40×0.30×0.10 mm) is orthorhombic, $a = 1649.1(3)$, $b = 1661.6(3)$, $c = 996.1(2)$ pm, $V = 2.7294(9)$ nm^3, space group $Pna2_1$, $Z = 4$, d_{calc} = = 1.179 g cm^{-3}, $\mu = 0.213$ mm^{-1}, $\lambda = 71.073$ pm, $F(000) = 1024$, STOE IPDS diffractometer, θ range for data collection, 2.38 to 23.49°, index ranges, $-18 \le h \le 18$, $-18 \le k \le 18$, $-11 \le l \le 11$, reflections collected 15151, independent reflections 4042 ($R_{int} = 0.1537$), completeness to $\theta = 23.49°$ 100.0%, max. and min. transmissions, 0.9790 and 0.9195; refinement method full-matrix least-squares on F^2, data/restraints/parameters 4042/4/331, Goodness-of-fit on F^2 0.853, final R indices $[I > 2\sigma(I)]$ $R_1 = 0.0665$, $wR_2 = 0.1208$, R indices (all data) $R_1 = 0.1490$, $wR_2 = 0.1448$, the structure was refined as a racemic twin with a fractional contribution of the main component 0.52(17), largest diff. peak and hole 0.399 and –0.225 eÅ^{-3}. The structure was solved by direct methods, the subsequent least-squares refinement located the positions of the remaining atoms in the electron density maps. All non-hydrogen atoms were refined with individual anisotropic deflection parameters. H atoms were calculated with common isotropic temperature factors. All calculations were performed with the SHELX program package.[6] Figure 1 was drawn with the use of the DIAMOND program.[7]

Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). These data can be obtained free of charge *via* www.ccdc.cam.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk). Any request to the CCDC for data should quote the full literature citation and CCDC reference number 227402. For details, see ‘Notice to Authors’, *Mendeleev Commun.*, Issue 1, 2003.

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