

Reactions of π -electron rich 1,2,4-triazines with organolithium nucleophiles

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3,5-Bis(trimethylsilyloxy)-1,2,4-triazine **1** and 3-methylthio-5-methoxy-1,2,4-triazine **6** were subjected to reactions with organolithium reagents at low temperatures. An unexpected regioselectivity in the addition of butyllithiums to **1**, which was strongly dependent on the temperature and substituents, was observed. For phenyllithium there was competition between N(1)–C(6) addition and C(5) substitution. No addition of butyllithiums to **6** was detected, only isolated reaction products showing zwitterionic structures.

Introduction

Recently we have reported that π -electron deficient 6-azauracil derivatives (1,2,4-triazine-3,5-diones) while reacting with *tert*-butyllithium or LDA underwent either Lewis acid promoted ring contraction or the addition of an organolithium reagent to the double carbon–nitrogen bond.¹ We have also attempted the lithiation of 6-azauracils *via* both deprotonation and lithium–bromine exchange, but under the conditions used, the desired overall electrophilic substitution reaction did not occur. The high reactivity of 1,2,4-triazines towards nucleophilic addition^{2,3} makes the lithiation of these compounds more difficult than for diazines.^{4–6} The first *ortho*-directed metalation of 1,2,4-triazine derivatives has been performed quite recently.⁷ We have found, however, that nucleophilic addition of *tert*-butyllithium to the nitrogen–carbon bond of 1,2,4-triazine followed by hydration can proceed through two different paths to give two isomeric compounds.¹ Therefore, we have expanded our study to the reactions of π -electron rich 6-azauracil derivatives with different organolithium reagents.

Results and discussion

We report in this paper the differences in the behavior of 1,2,4-triazines **1** and **6** toward organolithium agents on varying the temperature and the character of the organolithium nucleophiles.

The reaction of 3,5-bis(trimethylsilyloxy)-1,2,4-triazine (compound **1**) with different organolithium agents, such as *n*-butyllithium, *tert*-butyllithium and phenyllithium, gave no products arising from lithiation by abstraction of a weak acidic proton. The only reaction undergone by both *n*-butyllithium and *tert*-butyllithium is the addition reaction to a carbon–nitrogen bond. Organolithium reagents had evidently acted in general as nucleophiles rather than as lithiating agents (Scheme 1).

The formation of two isomeric adducts **2** and **3** with the predominance of compounds **3a** and **3b** was surprising. A polar addition mechanism is suggested, but a single electron transfer (SET) mechanism should also be considered. Compound **1** has two unsubstituted nitrogen atoms N(1) and N(2) able to bind Li⁺. Moreover, the neighbouring nitrogens in the 1,2,4-triazines enable the formation of a bridged complex that exhibits enhanced stability, where the Li⁺ bridges the N(1) and N(2)

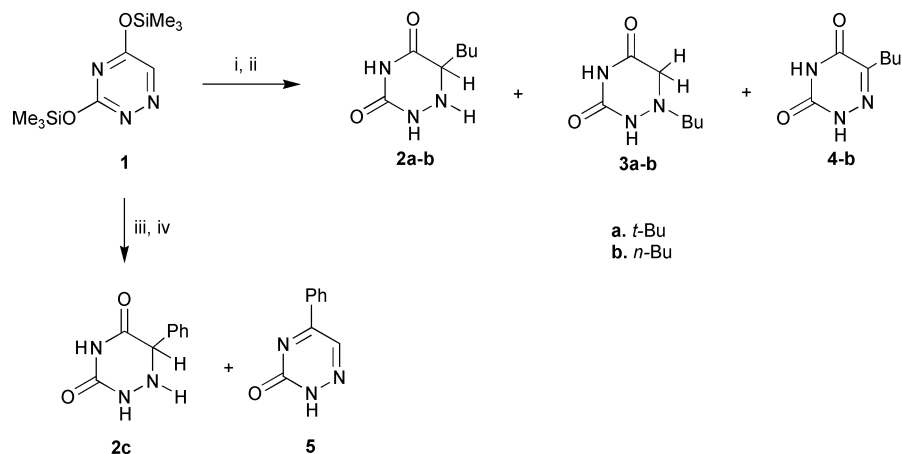
positions. The preference for the bridging conformation is a result of stronger polarisation of the ring nitrogens and a more efficient contribution of the lithium p orbitals.⁸ Such an intermediate could easily undergo nucleophilic attack at C(6) giving normal isomers **2a,b**, or at the N(1) position giving unexpected isomers **3a,b**. Following the lithiation at the two different nitrogens *via* the three centred complex we propose a polar addition mechanism to account for the products **2** and **3** respectively (Scheme 2).

We believe that the result can be explained in terms of the HSAB⁹ principle *if* the N(2) nucleophilic centre in the bridged complex is assumed to be harder than the N(1) position. Irrespective of the steric hindrance at C(3), attack by the hard Li⁺ at the harder site becomes competitive and creates an electrophilic, soft (or eventually borderline) site at N(1). Attack by the butyl anions, considered as soft bases, occurs exclusively at this site.

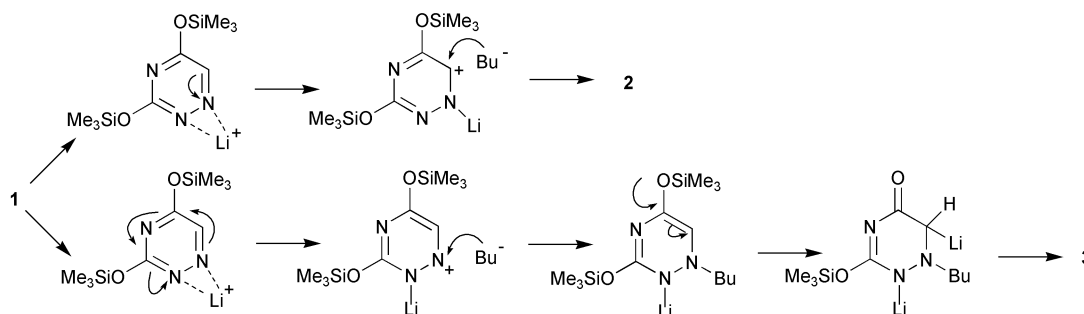
The alternative SET mechanism would involve electron transfer from butyllithium to compound **1** and the formation of a radical pair in the solvent cage. The normal addition products **2a,b** should arise from the caged species by radical combination, whereas compounds **3a,b** should arise from the reaction of butyl radicals that have “escaped” from the solvent cage. The addition of a free butyl radical to a neutral moiety of **1** followed by electron transfer, then association with Li⁺ and subsequent protonation affords the unexpected isomers **3a,b**.

The reactions with *tert*-butyllithium and *n*-butyllithium proceeded either alone or in combination with a Lewis acid, giving two isomeric adducts **2** and **3**. For the reaction of **1** with *tert*-butyllithium carried out at –100 °C the predominance of the unexpected compound **3a** is overwhelming; the ratio of **3a** : **2a**, based on the ¹H-NMR spectra of the isolated crude fraction, is 3.3 : 1. However, when the reaction was carried out at –20 °C the compounds were isolated in a ratio **3a** : **2a** of 1 : 2.3. For compounds **2b** and **3b**, isolated from the reaction of **1** with *n*-butyllithium at –100 °C, such a distinct difference in the quantities of the two adducts was not visible, but still the ratio of **3b** : **2b** is 1.3 : 1 and changes to 1 : 2.1 when the reaction was carried out at –20 °C. This suggests that temperature is the major factor in controlling the initial selectivity of the lithiation of the nitrogens. At low temperatures compound **3a** seems to be thermodynamically favored whereas **3b** is both kinetically and thermodynamically favored.

Quite a large amount of compound **4** was separated as a



Scheme 1 Reagents and conditions: i. BuLi, THF, $-100\text{ }^{\circ}\text{C}$ and $-20\text{ }^{\circ}\text{C}$ respectively; ii. H_2O ; iii. PhLi, $\text{B}(\text{OEt})_3$, THF, $-100\text{ }^{\circ}\text{C}$ and $-20\text{ }^{\circ}\text{C}$ respectively; iv. H_2O .



Scheme 2 Mechanistic pathways for the formation of compounds **2** and **3**.

product of the addition of *n*-butyllithium to **1** and subsequent loss of LiH. No traces of a similar product were observed in the reaction of *tert*-butyllithium with **1** carried out under the same conditions.

The competitive reactions of nucleophilic addition to a carbon–nitrogen bond of **1** are not general. When the reaction of compound **1** was carried out at $-100\text{ }^{\circ}\text{C}$ with phenyllithium in the absence of a Lewis acid, no addition reaction occurred under the conditions used. However, the reaction proceeded in the presence of triethyl borate as a mild Lewis acid giving two products **2c** and **5**. Triethyl borate is not a typical, commonly used Lewis acid, as, for example, boron trifluoride is preferred for phenyllithium activation in arylation reactions and in addition to double bonds.^{10,11} However, we have used it successfully in some of our syntheses, for instance as a good coordinating agent in ring contraction reactions.¹ The reaction, activated by triethyl borate, is strongly dependent on temperature. When the reaction of compound **1** with phenyllithium was carried out at $-100\text{ }^{\circ}\text{C}$ in the presence of triethyl borate, we obtained mainly product **2c**, whereas product **5** was formed in a negligible amount. When compound **1** was subjected to the reaction with phenyllithium at $-20\text{ }^{\circ}\text{C}$ compound **5** was obtained as the major product with a minor amount of product **2c**. Attempts at arylation of compound **1** by the activation with boron trifluoride gave a comparable result.

At $-100\text{ }^{\circ}\text{C}$ the N(1)–C(6) addition reaction affords a single regioisomer, no traces of the second isomeric product of addition to the nitrogen–carbon bond were detected which may be explained by the weaker nucleophilicity of phenyllithium. At $-20\text{ }^{\circ}\text{C}$ N(4) lithiation took place in spite of the strong hindering effect of two bulky trimethylsilyl groups. This intermediate facilitates nucleophilic attack at C(5) giving compound **5**. The structure of compound **5** was established by NMR and mass spectrometry and by X-ray analysis. Fig. 1 shows the structure of molecule **5**, and its crystal data are listed in Table 1. A simple mechanistic pathway for the formation of compound **5** is given in Scheme 3.

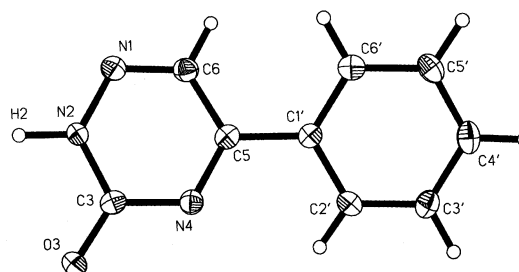
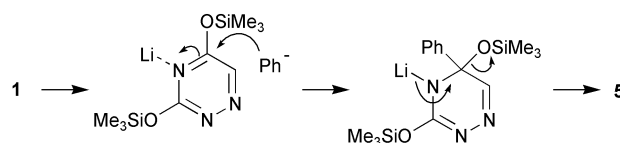


Fig. 1 Molecule **5** as present in the crystalline phase at 90 K. The thermal ellipsoids have been drawn at the 50% probability level.



Scheme 3 The mechanistic pathway for the formation of compound **5**.

The attempts to obtain products by electrophilic substitution of compound **1** and its 6-bromo derivative were unsuccessful.

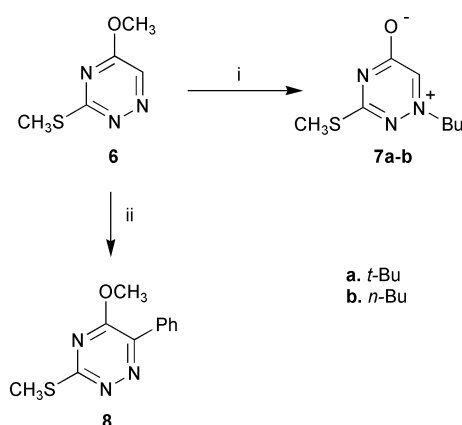
Nevertheless, we tried to investigate the relationship between substitution and addition to π -electron rich derivatives of 6-azauracil. For this purpose we obtained 3-methylthio-5-methoxy-1,2,4-triazine (compound **6**). This compound was prepared in a moderate yield *via* sulfur compounds.¹²

Compound **6** was subjected to reactions with *n*-butyllithium, *tert*-butyllithium and phenyllithium in the presence of triethyl borate acting as an activating agent and, at the same time, as an electrophile, at $-100\text{ }^{\circ}\text{C}$ and under similar conditions to those of the reactions of compound **1** described above. We could expect both competition between the formation of two adducts and competition between electrophilic substitution promoted by *ortho* directing methoxy groups and nucleophilic addition. In fact, reactions with butyllithiums proceeded without any

Table 1 Crystal data and structure refinement for **5** and **7a**

	5	7a
Empirical formula	C ₉ H ₇ N ₃ O	C ₈ H ₁₃ N ₃ OS
Formula weight	173.18	199.27
Temperature/K	90(1)	293(2)
Wavelength/Å	0.71073	0.71073
Crystal system, space group	Monoclinic, C2/c	Monoclinic, P2 ₁ /c
Unit cell dimensions		
<i>a</i> /Å	20.708(3)	8.877(2)
<i>b</i> /Å	6.9640(10)	5.8520(10)
<i>c</i> /Å	12.305(2)	19.624(4)
β /deg	117.01(3)	101.84(3)
Volume/Å ³	1581.0(4)	997.7(3)
Z, Calculated density/g cm ⁻³	8, 1.455	4, 1.327
Data / restraints / parameters	1579 / 0 / 141	2666 / 0 / 146
Goodness-of-fit on <i>F</i> ²	1.470	1.267
Final <i>R</i> indices [<i>I</i> > 2 σ (<i>I</i>)]	<i>R</i> 1 = 0.0472, <i>wR</i> 2 = 0.0632	<i>R</i> 1 = 0.0513, <i>wR</i> 2 = 0.0964

markedly detectable competition and gave the only isolable products **7a** and **7b** in fair yields. The reaction of compound **6** with phenyllithium furnished exclusively product **8** as the product of the expected normal addition to the nitrogen–carbon bond followed by the subsequent elimination process (Scheme 4).



Scheme 4 Reagents and conditions: i. BuLi, THF, B(OEt)₃, –100 °C; ii. PhLi, B(OEt)₃, THF, –100 °C.

However, confirmation of the structure of crystalline compound **7a** and oily compound **7b** by spectroscopic methods was ambiguous. In the UV spectra of **7a** we determined absorption bands at long wavelengths in several solvents (water, methanol, acetonitrile and chloroform) and we noticed that with decreasing solvent polarity the absorption bands shift to lower energies ($\lambda_{\text{max}}(\text{H}_2\text{O}) = 311 \text{ nm}$, $\lambda_{\text{max}}(\text{CH}_3\text{OH}) = 319 \text{ nm}$, $\lambda_{\text{max}}(\text{CH}_3\text{CN}) = 320 \text{ nm}$ and $\lambda_{\text{max}}(\text{CHCl}_3) = 328 \text{ nm}$). Such a solvent effect is characteristic of the band associated with an electronic transition from the ground state with a high dipole moment to an excited state with a lower dipole moment.^{13,14} UV spectra of **7a** recorded in a wide pH range showed the protonation of the compound at lower pH. Significant solvatochromism and the pH dependent spectra of compound **7a** showed its strongly polar structure, which was confirmed by X ray analysis. Molecule **7a** in the crystal state is shown in Fig. 2, and its crystal data are listed in Table 1.

The observed structure indicates that the molecule is a zwitterion with the positive charge at N(1) and the negative pole at O(5). Zwitterionic derivatives of 1,2,4-triazines are known in the literature and were derived from triazinium iodides by thermolysis.^{15,16}

The obtained compounds **7a** and **7b** distinctly show that at a low temperature triazine **6**, in the presence of butyllithiums, prefers lithiation at the N(2) position and, as a consequence, N(1) alkylation. In the case of arylation of compound **6**

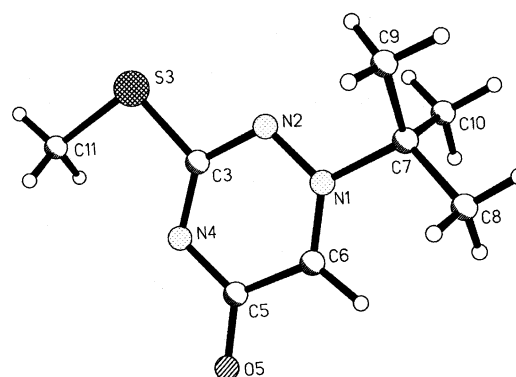


Fig. 2 The molecule of **7a** as present in the crystalline phase.

accomplished with phenyllithium, the reaction leads to the C(6) nucleophilic substitution (as an addition–elimination process) of a considerably weaker nucleophile giving compound **8**.

Conclusion

Usually the addition reactions of highly reactive organolithium reagents to carbon–nitrogen double bonds afford single regioisomers. We showed that the seemingly simple reactions of butyllithiums and phenyllithium with π -electron rich 6-azauracil derivatives followed by hydration gave unexpected products. Reactions of 3,5-bis(trimethylsilyloxy)-1,2,4-triazine with *n*-butyl and *tert*-butyllithium exhibit temperature dependent competition between attack at the C(6) and N(1) atoms giving two regioisomeric products of normal and unusual addition. Analogous reactions of 3-methylthio-5-methoxy-1,2,4-triazine with these reagents show the total regioselectivity of nucleophilic attack at the N(1) position and give exclusively the zwitterionic alkylation products. Reactions of both triazines with phenyllithium in general show the regioselectivity of the nucleophilic attack to be at the C(6) position.

Experimental

General

Melting points were determined on a Boetius apparatus and are reported uncorrected. All ¹H-NMR and ¹³C-NMR spectra were recorded on a Varian Gemini 300 MHz spectrometer in CDCl₃ and DMSO-*d*₆. Chemical shifts δ are reported in ppm downfield from an internal SiMe₄ standard. The UV spectra were recorded on a UV-2101PC Shimadzu spectrophotometer. The mass spectra were recorded on a AMD 402 spectrometer, ionisation was achieved through electron impact (EI) and fast atom bombardment (FAB). High resolution data were

obtained on the same instrument using a peak matching technique. The elemental compositions of the discussed ions were determined with an error of less than 10 ppm in relation to perfluorokerosene at a resolving power of 10000. The elemental analyses were made on a Perkin-Elmer apparatus. Tetrahydrofuran was distilled from sodium hydrate immediately before use. All reactions were carried out under an argon atmosphere using standard conditions for exclusion of moisture. The reaction temperature $-100\text{ }^{\circ}\text{C}$ was achieved by cooling with a N_2 /hexane bath. 3,5-Bis(trimethylsilyloxy)-1,2,4-triazine **1**¹⁷ and 3-methylthio-5-methoxy-1,2,4-triazine **6**¹² were obtained according to literature methods. 1.5 M *tert*-Butyllithium in pentane, 1.6 M *n*-butyllithium in hexanes and 1.8 M phenyllithium in cyclohexane : ether 70 : 30 were purchased from Aldrich.

X-Ray crystallography

Experimental and crystal data are listed in Table 1. Data for **5** and **7a** were measured on a KUMA KM4-CCD diffractometer. The crystal of **5** was investigated at 90 K, mainly to optimize the measurement conditions for the small sample. The structure was solved by direct methods, and all the hydrogen atoms were located from difference Fourier maps and refined by isotropic temperature factors. The angle between the molecular rings is $19.6(3)^{\circ}$. The molecules are linked by a pair of NH–O hydrogen bonds into dimers. The hydrogen-bond dimensions are: H(2)–O(3i) 1.78(2) Å, N(2) \cdots O(3i) 2.787(2) Å, N(2)–H(2)–O(3i) $176(1)^{\circ}$, symmetry code (i) $-x, y, 0.5 - z$. In **7a** the structure was solved by direct methods, the hydrogen at C(6) was located from a difference Fourier map and refined by an isotropic thermal parameter; the methyl hydrogens were calculated from the molecular geometry and allowed to rotate as rigid groups about the C–C or C–S pivoting bonds. Full data have been deposited at the Cambridge Crystallographic Data Centre.†

General procedure for reactions of 3,5-bis(trimethylsilyloxy)-1,2,4-triazine **1** with butyllithiums

3,5-Bis(trimethylsilyloxy)-1,2,4-triazine (2.3 g, 8.9 mmol) was dissolved in dry, THF (80 ml) and cooled to $-100\text{ }^{\circ}\text{C}$ under an argon atmosphere, using a N_2 /hexane bath. A solution of butyllithium (2.1 mol equivalent) was injected through a septum at such a rate that the internal temperature did not exceed $-90\text{ }^{\circ}\text{C}$. The temperature was decreased to $-100\text{ }^{\circ}\text{C}$, the reaction mixture kept at this temperature for 30 minutes and then it was allowed to warm to room temperature over a period of 3 h. The solution was evaporated to dryness under reduced pressure and then water was added (40 ml). The aqueous solution was acidified with 1 M HCl to pH 2–3. The solution was exhaustively extracted with a mixture of CHCl_3 : MeOH 4 : 1 v/v and the combined extracts were dried over MgSO_4 . The solvents were removed and the mixture of crude products was separated by column chromatography.

Reactions at $-20\text{ }^{\circ}\text{C}$ were carried out using the same procedure described above except for the temperature conditions. Regioselectivity ratios for both the low and high temperature reactions were obtained on the basis of ^1H NMR spectra of the crude products.

Reaction of **1 with *tert*-butyllithium¹.** The crude solid mixture was separated by column chromatography on silica gel with CH_2Cl_2 and then with CH_2Cl_2 : CH_3OH 25 : 1 v/v to yield compound **3a** (556 mg, 36%) and compound **2a** (124 mg, 8%) as white crystals.

2a: Mp $222\text{--}225\text{ }^{\circ}\text{C}$ (Found C, 49.33; H, 7.79; N, 24.81. $\text{C}_7\text{H}_{13}\text{N}_3\text{O}_2$ requires C, 49.11; H, 7.65; N, 24.55%); MS (EI)

m/z 171 (7) $[\text{M}]^+$, 115 (100) and 57 (56); HRMS: calculated for $\text{C}_7\text{H}_{13}\text{N}_3\text{O}_2$ 171.1008, found 171.1004; ν_{max} (KBr) 3205, 3083, 1735 and 1694 cm^{-1} ; δ_{H} (DMSO- d_6) 10.14 and 8.67 (2H, s, NH), 5.55 (1H, d, $J = 6.0\text{ Hz}$, N(1)H), 2.88 (1H, d, $J = 6.0\text{ Hz}$, C(6)H) and 1.00 (9H, s, C– CH_3); δ_{C} (DMSO- d_6) 171.7, 154.0, 64.3, 33.5 and 27.5.

3a: Mp $210\text{--}212\text{ }^{\circ}\text{C}$ (Found C, 49.14; H, 7.80; N, 24.69. $\text{C}_7\text{H}_{13}\text{N}_3\text{O}_2$ requires C, 49.11; H, 7.65; N, 24.55%); MS (EI) m/z 171 (12) $[\text{M}]^+$, 115 (23) and 57 (100); MS (FAB) m/z 172 $[\text{M} + 1]^+$; HRMS: calculated for $\text{C}_7\text{H}_{13}\text{N}_3\text{O}_2$ 171.1008, found 171.1012; ν_{max} (KBr) 3257, 3183, 3052, 1725 and 1695 cm^{-1} ; δ_{H} (DMSO- d_6) 10.35 and 9.06 (2H, s, NH), 3.60 (2H, s, C(6) H_2) and 1.03 (9H, s, C– CH_3); δ_{C} (DMSO- d_6) 171.0, 153.1, 59.1, 48.4 and 26.0.

Reaction of **1 with *n*-butyllithium.** The crude yellow oil was separated by column chromatography on silica gel using CH_2Cl_2 as eluent and then CH_2Cl_2 : CH_3OH 25 : 1 v/v to yield compound **2b** (244 mg, 16%), compound **4b** (120 mg, 8%) and compound **3b** (23% based on the ratios from ^1H -NMR spectra). Unfortunately compound **3b** undergoes slow decomposition on silica gel. We were not able to obtain absolutely pure compound **3b** for the melting point and HRMS determinations even after fine work-up and separation using preparative TLC plates.

2b: Mp $212\text{--}215\text{ }^{\circ}\text{C}$ (Found C, 49.04; H, 7.93; N, 24.78. $\text{C}_7\text{H}_{13}\text{N}_3\text{O}_2$ requires C, 49.11; H, 7.65; N, 24.55%); MS (EI) m/z : 171 (42) $[\text{M}]^+$, 114 (77), 86 (100) and 71 (32); HRMS: calculated for $\text{C}_7\text{H}_{13}\text{N}_3\text{O}_2$ 171.1008, found 171.1000; δ_{H} (DMSO- d_6) 10.14 and 8.72 (2H, s, NH), 5.44 (1H, d, $J = 8.24\text{ Hz}$, N(1)H), 3.18 (1H, m, C(6)H), 1.39 (2H, m, C(6)– CH_2 –), 1.30 (4H, m, C(6)– $\text{C-CH}_2\text{CH}_2$ –) and 0.86 (3H, t, $J = 7.1\text{ Hz}$, C(6)– $\text{C-CH}_2\text{CH}_2$ –); δ_{C} (DMSO- d_6) 13.9, 21.9, 26.9, 27.7, 57.0, 154.0 and 173.0.

3b: δ_{H} (DMSO- d_6) 10.41 and 9.27 (2H, s, NH), 3.56 (2H, s, C(6) H_2), 2.63 (2H, t, $J = 7.1\text{ Hz}$, N(1)– CH_2 –), 1.2–1.4 (4H, m, N(1)– $\text{C-CH}_2\text{CH}_2$ –) and 0.88 (3H, m, N(1)– C-C-CH_3).

4b: MS (EI) m/z : 169(26) $[\text{M}]^+$, 149 (51), 127 (100), 112 (9), 83 (21) and 56 (24); HRMS: calculated for $\text{C}_7\text{H}_{11}\text{N}_3\text{O}_2$ 169.0851, found 169.0861; δ_{H} (DMSO- d_6) 12.03 and 11.85 (2H, s, NH), 2.43 (2H, t, $J = 7.7\text{ Hz}$, C(6)– CH_2 –), 1.30 and 1.49 (4H, m, C(6)– $\text{C-CH}_2\text{CH}_2$ –) and 0.88 (3H, t, $J = 7.4\text{ Hz}$, C(6)– C-C-CH_3); δ_{C} (DMSO- d_6) 13.8, 21.8, 28.0, 28.8, 145.2, 149.4 and 157.1.

Reaction of 3,5-bis(trimethylsilyloxy)-1,2,4-triazine **1 with phenyllithium at $-100\text{ }^{\circ}\text{C}$.** 3,5-Bis(trimethylsilyloxy)-1,2,4-triazine (950 mg, 3.7 mmol) was dissolved in dry, freshly distilled THF (40 ml) and cooled to $-100\text{ }^{\circ}\text{C}$ under an argon atmosphere, using a N_2 /hexane bath. A solution of phenyllithium (1.8 M solution, 6.2 ml, 11.1 mmol) was injected through a septum at such a rate that the internal temperature did not exceed $-80\text{ }^{\circ}\text{C}$. The temperature was decreased to $-100\text{ }^{\circ}\text{C}$ and triethyl borate (1.9 ml, 11.1 mmol) was added to the brownish solution. The reaction mixture was kept at this temperature for 30 minutes and then was allowed to warm to room temperature over a period of 3 h. The solution was evaporated to dryness under reduced pressure and then water was added (40 ml). The aqueous solution was acidified with 1 M HCl. The solution was extracted with hexane to remove non-polar impurities and then extracted with CHCl_3 (3 \times 30 ml). Combined CHCl_3 fractions were dried over MgSO_4 , the solvent was evaporated and the crude product obtained was crystallized from EtOH giving compound **5** (6.4 mg, 1%). After 24 hours a white precipitate appeared which was filtered off and dried. The obtained crude adduct containing traces of 6-azauracil was crystallized from a mixture of AcOEt with small amount of EtOH giving pure compound **2c** (127mg, 18%).

We did not recover residues of 6-azauracil remaining in the aqueous solution.

† CCDC reference numbers 181717 (**5**) and 181716 (**7a**). See <http://www.rsc.org/suppdata/p1/b2b205058g/> for crystallographic files in .cif or other electronic format.

Reaction of 3,5-bis(trimethylsilyloxy)-1,2,4-triazine 1 with phenyllithium at -20°C . Reactions at -20°C were carried out using the same procedure described above except for temperature and the extractive work-up. The aqueous acidic solution was extracted with hexane to remove non-polar impurities and then exhaustively extracted with a mixture of CHCl_3 : MeOH 4 : 1 v/v. Combined extracts were dried over MgSO_4 . The solvent were removed and the mixture of crude products was separated by column chromatography with CH_2Cl_2 and then with CH_2Cl_2 : CH_3OH 25 : 1 v/v to yield compound **5** (198 mg, 31%) and compound **2c** (56 mg, 8%). Compound **5** for X-ray studies was crystallized from H_2O .

2c: Mp $240\text{--}242^{\circ}\text{C}$ (Found C, 56.46; H, 4.74; N, 21.74. $\text{C}_9\text{H}_9\text{N}_3\text{O}_2$ requires C, 56.54; H, 4.74; N, 21.98%); MS (EI) m/z : 191 (3) $[\text{M}]^+$, 162 (1), 120 (2), 113 (55), 104 (10), 70 (22) and 42 (100); HRMS: calculated for $\text{C}_9\text{H}_9\text{O}_2\text{N}_3$ 191.0695, found 191.0703; δ_{H} (DMSO- d_6) 10.46 and 8.89 (2H, s, NH), 7.39 (5H, m, Ph), 6.13 (1H, d, $J = 5.8$ Hz, N(1)H) and 4.54 (1H, d, $J = 5.5$ Hz, C(6)H), (DMSO- d_6 + D_2O) 7.39 (5H, m, Ph) and 4.55 (1H, s, C(6)H); δ_{C} (DMSO- d_6) 60.1, 128.17, 128.24, 128.57, 129.60, 153.9 and 171.5.

5: Mp $133\text{--}135^{\circ}\text{C}$ (Found C, 62.17; H, 4.04; N, 24.00. $\text{C}_9\text{H}_7\text{N}_3\text{O}$ requires C, 62.42; H, 4.07; N, 24.26%); MS (EI) m/z : 173 (100) $[\text{M}]^+$, 145 (1.6), 131 (2.5), 102 (84), 89 (20) and 77 (10); HRMS: calculated for $\text{C}_9\text{H}_7\text{N}_3\text{O}_2$ 189.0538, found 189.0531; δ_{H} (DMSO- d_6) 13.36 (1H, s, NH), 8.74 (1H, s, C(6)H), 8.22 (2H, m, Ph) and 7.65 (3H, m, Ph), (DMSO- d_6 + D_2O) 8.72 (1H, s, C(6)H), 8.21 (2H, m, Ph) and 7.69 (3H, m, Ph); δ_{C} (DMSO- d_6) 128.4, 129.3, 131.2, 133.274, 133.293, 154.1 and 164.5.

General procedure for reactions of 3-methylthio-5-methoxy-1,2,4-triazine 6 with butyllithiums and phenyllithium

Compound **6** (400mg, 2.6 mmol) was dissolved in dry, freshly distilled THF (30 ml) and cooled to -100°C under an argon atmosphere. A solution of alkylolithium (7.8 mmol) was injected through a septum at such a rate that the internal temperature did not exceed -90°C . The temperature was decreased to -100°C and triethyl borate (1.33 ml, 7.8 mmol) was injected. The reaction mixture was kept at this temperature for an additional 30 minutes and then was slowly allowed to warm to room temperature. The solution was evaporated to dryness under reduced pressure and water was added (30 ml) and the aqueous solution was acidified with 1 M HCl. The solution was extracted with CHCl_3 (3×20 ml), the combined organic layer was dried over Na_2SO_4 and solvent was evaporated to dryness giving an oily residue. The crude products were purified by column chromatography.

Reaction of 6 with *tert*-butyllithium

The crude mixture was separated by column chromatography on silica gel with hexane : CHCl_3 1 : 0–0 : 1 v/v. Crystallization from AcOEt yielded compound **7a** (124 mg, 24%) as pale yellow crystals.

7a: Mp $232\text{--}233^{\circ}\text{C}$ (Found C, 48.41; H, 6.52; N, 21.06. $\text{C}_8\text{H}_{13}\text{N}_3\text{OS}$ requires C, 48.22; H, 6.57; N, 21.09%); MS (EI)

m/z : 199 (22) $[\text{M}]^+$, 143 (54), 115 (11), 57 (100) and 41 (62); δ_{H} (DMSO- d_6) 8.11 (1H, s, C(6)H), 2.42 (3H, s, S- CH_3) and 1.58 (9H, s, N(1)-*tert*-Bu); δ_{C} (DMSO- d_6) 174.3, 163.9, 133.6, 71.2, 27.5 and 12.7.

Reaction of 6 with *n*-butyllithium

The product was isolated by column chromatography on silica gel with CHCl_3 : CH_3OH 1 : 0–25 : 1 v/v to yield compound **7b** (83 mg, 16%) as a colorless oil.

7b: MS (EI) m/z : 199 (3) $[\text{M}]^+$, 167 (43), 148 (100), 115 (3) and 57 (39); HRMS calculated for $\text{C}_8\text{H}_{13}\text{N}_3\text{OS}$: 199.07793, found 199.07631; δ_{H} (DMSO- d_6) 7.60 (1H, s, C(6)H), 4.13 (2H, t, $J = 7.2$ Hz, N(1)- CH_2), 2.51 (3H, s, S- CH_3), 1.98 and 1.38 (4H, m, N(1)- $\text{C}-\text{CH}_2\text{CH}_2$) and 0.99 (3H, t, $J = 7.3$ Hz, N(1)- $\text{C}-\text{C}-\text{CH}_3$); δ_{C} (CDCl_3) 13.5, 13.8, 14.2, 27.7, 69.8, 133.0, 153.5 and 163.9.

Reaction of 6 with phenyllithium

The residue was purified by column chromatography on silica gel with hexane : CHCl_3 1 : 0–0 : 1 and then CHCl_3 : CH_3OH 25 : 1 v/v to yield an oily compound **8** (85 mg, 14%) which solidified after a longer period of time.

8: (Found C, 56.47; H, 5.02; N, 17.72. $\text{C}_{11}\text{H}_{11}\text{N}_3\text{OS}$ requires C, 56.63; H, 4.75; N, 18.01%); MS (EI) m/z : 233 (100) $[\text{M}]^+$, 218 (10), 190 (2), 148 (5), 132 (76), 117 (36) and 89 (64); (FAB) m/z : 234 $[\text{M}^+ + 1]$; HRMS: calculated for $\text{C}_{11}\text{H}_{11}\text{ON}_3\text{S}$ 233.0623, found 233.0620; δ_{H} (DMSO- d_6) 8.01 (2H, m, Ph), 7.48 (3H, m, Ph), 4.10 (3H, s, O- CH_3) and 2.71 (3H, s, S- CH_3); δ_{C} (CDCl_3) 14.1, 54.6, 128.3, 128.8, 130.0, 132.2, 146.2, 159.5 and 170.0.

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