Ureas as new nucleophilic reagents for S_N^H amination and carbamoyl amination reactions in the 1,3,7-triazapyrene series

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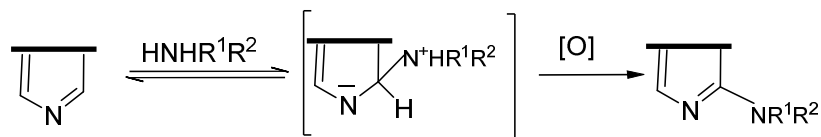*E-mail: ivborovlev@rambler.ru*

Abstract
The ability of urea anions to react as nucleophiles with 1,3,7-triazapyrenes has been investigated. It was found that, against all expectations, the products of the substitution of hydrogen (S_N^H) by an amino group were isolated in good yields. The reactions proceed in anhydrous DMSO solution at room temperature. However, when anions of mono substituted ureas containing bulky substituents were used, the products of previously unknown S_N^H reactions of alkyl carbamoyl amination were obtained.

Keywords: Nucleophilic aromatic substitution of hydrogen, amination, carbamoyl amination, 1,3,7-triazapyren-6-amines

Introduction

The synthesis of aromatic and heteroaromatic amines and their derivatives is still of great interest, due to their importance as building blocks for pharmaceuticals, agrochemicals, polymers, and materials.[1-4] The most common method for their preparation is nucleophilic aromatic substitution of halide or other nucleofugal groups under noncatalytic[5,6] or catalytic conditions.[7-10] In the case of electron-deficient substrates, such as azines and nitroarenes, the nucleophilic aromatic substitution of hydrogen (S_N^H),[11,12] including its oxidative[13-15] and vicarious[16,17] versions, is an attractive alternative. An oxidative nucleophilic substitution of hydrogen enables one to carry out the process following the principles of green chemistry, such as atom efficiency, shorter synthesis, less hazardous chemicals, waste prevention, etc.[18,19] This methodology does not require any preliminary introduction of a classical leaving group into an aromatic substrate or reagent and does not need expensive catalysts or ligands. Mechanistically, it consists of σ^H-adduct formation and its subsequent oxidative rearomatization (Scheme 1).

Scheme 1. Oxidative amination of azines.

As a rule, the second step is rate-limiting, because the hydride ion, which formally has to be lost, is a very poor leaving group. Numerous investigations have shown that spontaneous aromatization of such σ^H-complexes occurs quite rarely. Usually, elimination of hydride ion is strongly facilitated by adding a special external oxidant. In spite of continuing discussion regarding hydride ion elimination, the stepwise mechanism involving successive electron–proton–electron (EPE) transfer appears to be the most plausible pathway.[20] In the presence of KMnO$_4$ electron-deficient azines and nitroarenes can be smoothly aminated by potassium amide in liquid ammonia or with liquid ammonia itself.[15]

In our previous reports, we have shown that 1,3,7-triazapyrene (**1a**) displays special properties due to the unique fusion of the carbocyclic and heterocyclic rings. These properties include an unusual ease of oxidative nucleophilic substitution of hydrogen, such as hydroxylation,[21] alkoxylation,[22,23] amination,[21] alkylamination,[24] arylation,[25,26] arylamination[27] and even amidation.[28] Another unusual feature of 1,3,7-triazapyrenes is that the greater part of these transformations can be carried out in aqueous media. Note that *peri*-annelated azines, including 1,3,7-triazapyrene, are now of practical interest for electronic applications, especially as organic light-emitting diodes (OLEDs).[29,30]

It is known that the urea molecule is a weak electrophile and a weak ambident nucleophile. Ureas are normally rather inert towards alcohols, amines, and thiols: they require high temperatures, acidic or basic conditions, or metal catalysis, to undergo nucleophilic substitution reactions.[31-34] Ureas were used earlier as specific nitrogen nucleophiles in the palladium(II)-catalyzed amino carbonylation of unsaturated amines,[35] in intramolecular cyclisation of ureido acids and esters,[36] in the synthesis of a di- and triarylamines by interaction with unactivated aryl halides under palladium catalysis[37] and in Biginelli reactions.[38]
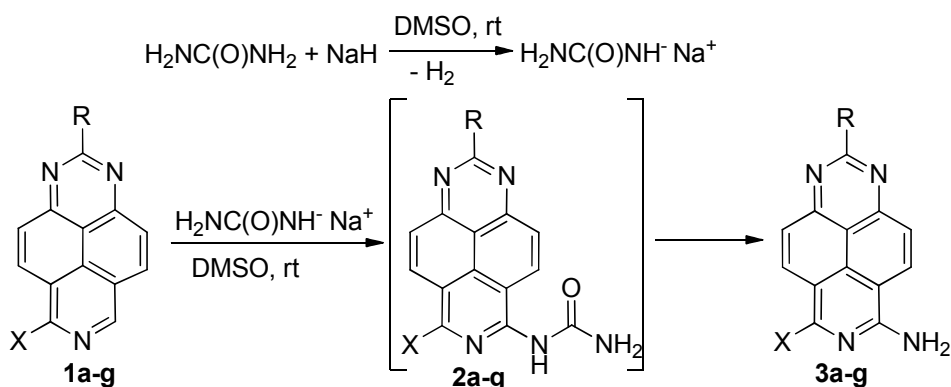
In the course of this study, and taking into account the results of oxidative nucleophilic amidation of 1,3,7-triazapyrene,[28] we have tested the possibility of S$_N^H$ carbamoyl amination of this heterocycle using urea as the nucleophilic reagent.

Results and Discussion

Firstly, we studied the reaction of 1,3,7-triazapyrene (**1a**) with urea. It does not occur in a wide temperature range neither in polar (DMSO, ethanol, acetonitrile), or in non-polar solvents (toluene, xylene). The obvious reason for this is the low nucleophilicity of the reagent. As in the cases of aryl amination[27] and amidation[28] reactions, in order to increase its nucleophilicity we generated a urea anion by the action of sodium hydride in anhydrous dimethyl sulfoxide.

It is known that DMSO is a versatile and powerful solvent which provides maximum nucleophilicity of an anionic nucleophiles due to the absence of the solvate shell. The use of DMSO makes it possible to carry out this reaction at room temperature, without isolation from the air oxygen.

As it turned out, the reaction product obtained after water addition was 1,3,7-triazapyren-6-amine (**3a**) instead of the expected (1,3,7-triazapyren-6-yl)-urea (**2a**) (Scheme 2, Table 1, Entry 1).

Scheme 2. S_N^H-Amination of 1,3,7-triazapyrenes **1a-g** by urea anion.

One can assume that the process progresses according to Scheme 2, but intermediate **2a** enters then the conversion process into amine **3a**, for example by alkaline hydrolysis during isolation.

Interestingly, though not being a strong nucleophile, the urea anion readily enters into an oxidative nucleophilic substitution of hydrogen with 1,3,7-triazapyrene. It appears that air oxygen is the oxidant for this reaction.

To confirm this, we performed the reaction in DMSO under argon. In this case only traces of product **3a** were detected by TLC. Moreover a mixture of oligomerization products was obtained where the starting 1,3,7-triazapyrene has reacted completely under these conditions.
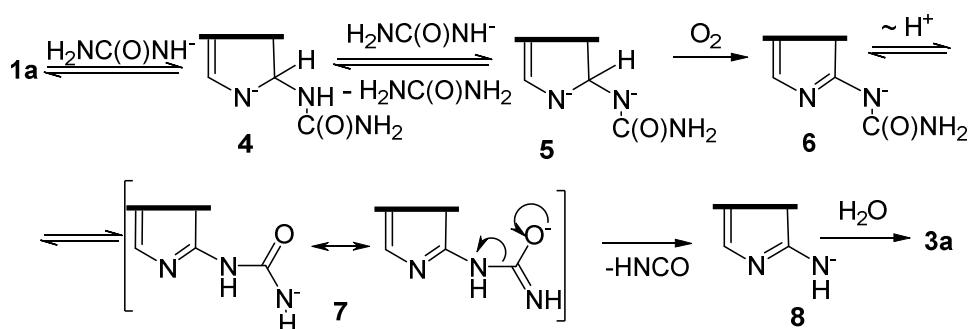
Thus, one can conclude that 1,3,7-triazapyrene itself is not an effective acceptor of hydride ion and the decisive factor for rearomatization of σ^H-adduct **4** is crucial access to air oxygen (Scheme 3). It is known that molecular oxygen is a very common oxidant for oxidation of σ^H-adducts; it appears however that it operates efficiently only in the cases where anionic σ^H-

adducts can be further deprotonated by a base present in the system; thus, it is the corresponding dianion that is actually oxidized.[12]

In accordance with this it can be assumed that carbamoyl amination of 1,3,7-triazapyrene involves the formation of σ^H-complex **4**, its subsequent NH-deprotonation and oxidative aromatization of the dianion **5** to the anion **6** (Scheme 3).

It is relevant to ask whether alkaline hydrolysis during isolation is the reason for the subsequent transformation of the intermediate **2a** into the final isolated product **3a**? To test this, we analyzed a sample of the reaction mixture before isolation, by high resolution mass spectrometry (HRMS). This detected the presence mainly of a molecular ion corresponding to product **3a**. The molecular ion of the intermediate **2a** was also observed, but with a small content. Note, that in a separate experiment we showed that in the absence of 1,3,7-triazapyrene, urea anion in DMSO no change occurs at room temperature over a long period.

We believe that the final step in the synthesis of amine **3a** includes the reversible conversion of anion **6** into anion **7** followed by elimination of 6-amino-1,3,7-triazapyrene anion **8** as a better leaving group in comparison with amide anion. Addition of water to the reaction mixture leads to protonation of the anion **8** to form product **3a** (Scheme 3).

Scheme 3. The postulated pathway for formation of compound **3a**.

So, in the absence of oxygen, neither σ^H-complex **4** nor dianion **5** are stable at room temperature and undergo oligomerization process. Repeated amination reaction does not occur because the anion **6** is not able to react further with nucleophiles. Thus the urea anion plays the dual role in this reaction acting as a nucleophilic agent and a base.

Amination of other 1,3,7-triazapyrenes in the system urea/NaH/DMSO produced similar results (Scheme 2, Table 1, Entries 2-8). 6-*p*-Tolyl- (**1b**), 6-(3,4-dimethylphenyl)-(**1c**), 6-*p*-methoxyphenyl- (**1d**), 6-*p*-ethoxyphenyl- (**1e**), 6-dimethylamino-(**1f**) and 2-methyl- (**1g**) 1,3,7-triazapyrenes also react under these conditions. The corresponding 6-amino-1,3,7-triazapyrenes (**3a-f**) were obtained in 65-88% yields. So the presence of neutral or even electron-donor substituents in the 1,3,7-triazapyrene ring does not block this process.

Table 1. Synthesis of 6-amino-1,3,7-triazapyrenes **3a-g**[a] in the system urea/NaH/DMSO by S_N^H process

Entry	Starting compound			Reagent	Reaction time (h)	Product	Yield (%)
	No	R	X				
1	**1a**	H	H	$H_2NC(O)NH^-$	5	**3a**	88
2	**1b**	H	$4\text{-}CH_3C_6H_4$	$H_2NC(O)NH^-$	27	**3b**	77
3	**1c**	H	$3,4\text{-}di(CH_3)C_6H_3$	$H_2NC(O)NH^-$	36	**3c**	69
4	**1d**	H	$4\text{-}CH_3OC_6H_4$	$H_2NC(O)NH^-$	3	**3d**	83
5	**1e**	H	$4\text{-}C_2H_5OC_6H_4$	$H_2NC(O)NH^-$	7	**3e**	86
6	**1f**	H	Me_2N	$H_2NC(O)NH^-$	11	**3f**	65
7	**1g**	Me	H	$H_2NC(O)NH^-$	2	**3g**	5
8	**1a**	H	H	$PhHNC(O)NH^-$	7	**3a**	57

[a]In all experiments the use of six equivalents of the corresponding urea and six equivalents of NaH was found to be optimal for these procedures.
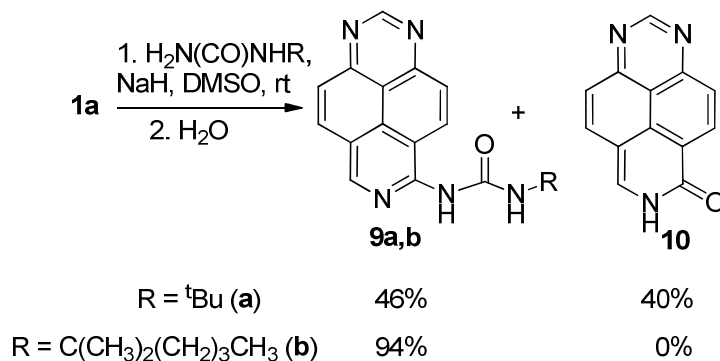
The exception in this series was 2-methyl-1,3,7-triazapyren-6-amine (**3g**), which was obtained with a yield of only 5%. In our opinion, this was caused by deprotonation of the 2-CH_3 group of the starting compound **1g** with subsequent oligomerization of the quinoid anion obtained. This process proceeds even faster in the absence of urea, i.e. in the system of compound **1g**/DMSO/NaH.

As expected, use of *N*-phenylurea instead of urea itself in the reaction with 1,3,7-triazapyrene (**1a**) led to same primary amine **3a** (Table 1, Entry 8).

Thus, according to the mechanism which is shown in Scheme 3 for the synthesis of compounds **3**, this is a novel version of oxidative S_N^H reactions. Its distinguishing feature is the spontaneous transformation of a nucleophilic group of the S_N^H product obtained, i.e. in our case converting of the carbamoyl amino group into the amino group. Therefore, the urea anion may be viewed as a new useful amination reagent for some π-deficient substrates.

Unexpected results were obtained upon using mono substituted ureas containing bulky substituents, such as *tert*-butylurea and (1,1-dimethylpentyl)urea [synthesized from 2-methylhexan-2-ol (see Experimental Section)]. Being an ambident nucleophile, the urea anion has served as a nitrogen nucleophile in the reactions discussed above. However, in the reaction of *tert*-butylurea anion with 1,3,7-triazapyrene (**1a**) two products were isolated: 1-*tert*-butyl-3-(1,3,7-triazapyren-6-yl)-urea (**9a**) and the earlier known 7*H*-1,3,7-triazapyren-6-one (**10**)[21] (Scheme 4). In contrast, the use of (1,1-dimethylpentyl)urea, which contains a more bulky

substituent, led under the same conditions to 1-(1,1-dimethylpentyl)-3-(1,3,7-triazapyren-6-yl)-urea (**9b**) as the sole product.
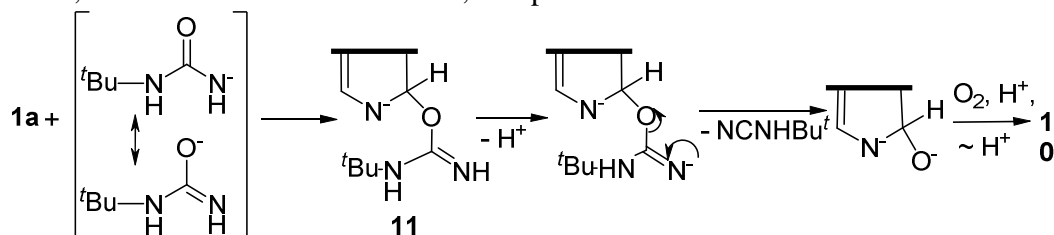

Scheme 4. The reaction of 1,3,7-triazapyrene (**1a**) with sterically hindered ureas at room temperature.

In contrast to the intermediates **2** (Scheme 2), compounds **9a,b** proved to be more stable than their analogs. The probable cause of their comparative stability is spatial interference for the deprotonation of NHR groups which is necessary for the further conversions according to Scheme 3. However, they are unstable when heated in the crystalline state and in solution. For example, both these compounds under slow heating above the melting temperature were quantitatively converted into 1,3,7-triazapyren-6-amine (**3a**). Our attempts to recrystallize compound **9a** from xylene, ethanol or benzene, as well as upon chromatographic separation on silica gel, led to partial transformation into amine **3a**. So, when a solution of 1-*tert*-butyl-3-(1,3,7-triazapyren-6-yl)-urea (**9a**) in xylene was refluxed for one hour, it was converted into 1,3,7-triazapyren-6-amine (**3a**) in 91% yield. Probably the process proceeds in accordance with Scheme 3 wherein the the pyridine type nitrogen atoms of 1,3,7-triazapyrene ring function as base.

Note, that the compounds **9a,b** represent the first example of the earlier unknown reaction of alkyl carbamoyl amination, i.e. the reaction of the direct oxidative nucleophilic substitution of hydrogen by an alkyl urea fragment.

The formation of compound **10** in the reaction with an anion of *tert*-butylurea indicates that it can react partly as O-nucleophile to form σ^H-complex **11**. As a result of the subsequent conversions, which are shown in Scheme 5, compound **10** is formed.

Scheme 5. The suggested route for 7*H*-1,3,7-triazapyren-6-one (**10**) formation.

The different behavior of the two sterically hindered ureas is probably the result of their different spatial conformations which undergo the reaction with 1,3,7-triazapyrene. In any case, when the reaction of 1,3,7-triazapyrene (**1a**) with (1,1-dimethylpentyl)urea anion was carried out at 70-75 °C only traces of product **9b** were detected by TLC and the sole isolated product was above-mentioned 7*H*-1,3,7-triazapyren-6-one (**10**) in 72% yield. Thus the chemoselectivity of the reactions involving the hindered ureas, i.e. whether they will react as N- or O-nucleophiles, depends upon the predominant conformer stability under the reaction conditions.

We have shown further that, as in the case of secondary benzamides,[28] 1,3-dimethyl urea, containing two secondary amido groups does not react with 1,3,7-triazapyrene under the same conditions. This is due to spatial hindrance for S_N^H adduct formation as well as the impossibility to obtain its dianion which could then be oxidized by air oxygen at the aromatization stage (Scheme 3).

Conclusions

We have shown that 1,3,7-triazapyren-6-amines can be easily obtained from 1,3,7-triazapyrenes through oxidative nucleophilic substitution of hydrogen, using the urea anion as reactant. Reactions proceed in anhydrous DMSO solution at room temperature without protection from the air. When monosubstituted ureas with bulky substituents were used the first products of the earlier unknown S_N^H reactions of alkyl carbamoyl amination were obtained.

Experimental Section

General. All melting points were determined in glass capillaries and are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance HD 400 spectrometer in the solvent indicated. The chemical shifts are given in parts per million (ppm) relative to residual solvent signals.[39] All coupling constants are in Hertz. High-resolution mass spectra (HRMS) were registered on a Bruker UHR-TOF Maxis[TM] Impact instrument using the ESI technique. IR spectra were recorded on a Shimadzu IRTracer-100 as thin films.
Starting compounds **1a,g**,[40] **1b,c**,[26] 1**d,e**,[25] and 1**f**[41] were obtained by known procedures. Sodium hydride as a 60% w/w dispersion in mineral oil was used as such (Merck). Other commercially available chemicals were also used without additional purification. The progress of the reactions was monitored by thin-layer chromatography (TLC), using Silufol UV-254 silica gel plates. The identification of samples from different experiments was accomplished by mixed mps or by superposition their IR spectra. Copies of the ^{1}H NMR, ^{13}C NMR and IR spectra of all new compounds are available as supporting information.

General Procedures for the Synthesis of 1,3,7-triazapyren-6-amines 3a-g

The reaction vessel must be protected from the air moisture, but not from air oxygen. To a solution of the corresponding urea (3 mmol) in anhydrous DMSO (5 mL), NaH (3 mmol, based on active ingredient) was added at rt. When hydrogen bubbling ceased, the corresponding 1,3,7-triazapyrene (**1a–g**; 0.5 mmol) was added. The mixture was stirred vigorously at rt during the time indicated in Table 1. Then H_2O (20 mL) was added and the precipitate obtained was filtered off, washed with H_2O and dried.

1,3,7-Triazapyrene-6-amine (**3a**). Brown solid (97 mg, 88%, using urea and 63 mg, 57%, using phenylurea), subl. p. 250 °C (from EtOH), ref.[21] 250 °C.

8-(4-Tolyl)-1,3,7-triazapyren-6-amine (**3b**). Yellow solid (119 mg, 77%), mp 265-266 °C (from EtOH). ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.45 (s, 3H, CH$_3$), 7.43 (d, J 7.9 Hz, 2H, H-3,5 Tol), 7.61 (d, J 9.3 Hz, 1H, H-4), 7.68 (d, J 7.9 Hz, 2H, H-2',6' Tol), 7.95 (d, J 9.2 Hz, 1H, H-10), 8.03 (br. s, 2H, NH$_2$), 8.33 (d, J 9.3 Hz, 1H, H-5), 8.90 (d, J 9.2 Hz, 1H, H-9), 9.43 (s, 1H, H-2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.0, 106.9, 113.3, 116.7, 120.8, 123.5, 128.9, 129.1, 130.4, 131.4, 135.1, 135.6, 138.6, 154.1, 155.4, 156.9, 157.5, 159.2. IR: 3425, 3308, 1636, 1614, 1598, 1574 cm^{-1}. HRMS (ESI): calculated for $C_{20}H_{15}N_4$ 311.1291; found 311.1297 [M + H][+].

8-(3,4-Dimethylphenyl)-1,3,7-triazapyren-6-amine (**3c**). Orange-colored solid (112 mg, 69%), mp 202-203 °C (from EtOH). ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.37 (s, 6H, 3- and 4-Me), 7.37 (d, J 7.8 Hz, 1H, H-5 C$_6$H$_3$), 7.48 (dd, J 7.7, J 1.2 Hz, 1H, H-6 C$_6$H$_3$), 7.57 (d, J 1.2 Hz, 1H, H-2 C$_6$H$_3$), 7.61 (d, J 9.3 Hz, 1H, H-4), 7.94 (d, J 9.2 Hz, 1H, H-10), 7.98 (br. s, 2H, NH$_2$), 8.35 (d, J 9.3 Hz, 1H, H-5), 8.91 (d, J 9.2 Hz, 1H, H-9), 9.42 (s, 1H, H-2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 19.3, 19.5, 106.8, 113.3, 116.7, 120.6, 123.3, 128.0, 129.0, 129.3, 131.4, 131.5, 135.3, 136.0, 136.3, 137.4, 154.1, 155.2, 156.9, 157.3, 159.4. IR: 3321, 3164, 3118, 1653, 1608 cm^{-1}. HRMS (ESI): calculated for $C_{21}H_{17}N_4$ 325.1448; found 325.1454 [M+H][+].

8-(4-Methoxyphenyl)-1,3,7-triazapyren-6-amine (**3d**). Pale brown solid (135 mg, 83%), mp 280-281 °C (from EtOH). ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.88 (s, 3H, OCH$_3$), 7.17 (d, J 8.6 Hz, 2H, H-3',5' C$_6$H$_4$), 7.59 (d, J 9.3 Hz, 1H, H-4), 7.75 (d, J 8.6 Hz, 2H, H-2',6' C$_6$H$_4$), 7.91 (d, J 9.2 Hz, 1H, H-10), 8.00 (br. s, 2H, NH$_2$), 8.35 (d, J 9.3 Hz, 1H, H-5), 8.88 (d, J 9.2 Hz, 1H, H-9), 9.40 (s, 1H, H-2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 55.3, 106.7, 113.2, 113.8, 116.8, 120.7, 123.3, 129.1, 130.8, 131.4, 132.0, 135.2, 154.2, 155.3, 156.8, 157.5, 158.8, 160.1. IR: 3435, 3332, 3190, 1638, 1600, 1576 cm^{-1}. HRMS (ESI): calculated for $C_{20}H_{15}N_4O$ 327.1240; found 327.1242 [M + H][+].

8-(4-Ethoxyphenyl)-1,3,7-triazapyren-6-amine (**3e**). Orange-colored solid (146 mg, 86%), mp 195-196 °C (from EtOH). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.40 (t, J 6.7 Hz, 3H, CH_3CH$_2$), 4.15 (q, J 6.7 Hz, 2H, CH$_3$CH_2), 7.15 (d, J 8.5 Hz, 2H, H-3,5 C$_6$H$_4$), 7.60 (d, J 9.3 Hz, 1H, H-4), 7.73 (d, J 8.5 Hz, 2H, H-2,6 C$_6$H$_4$), 7.92 (d, J 9.1 Hz, 1H, H-10), 8.00 (br. s, 2H, NH$_2$), 8.36 (d, J 9.3 Hz, 1H, H-5), 8.88 (d, J 9.1 Hz, 1H, H-9), 9.41 (s, 1H, H-2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 14.7, 63.3, 106.7, 113.2, 114.2, 116.8, 120.7, 123.3, 129.2, 130.6, 131.4, 132.0, 135.2, 154.2, 155.3, 156.8, 157.5, 158.8, 159.3. IR: 3444, 3342, 3236, 1638, 1601, 1501 cm^{-1}. HRMS (ESI): calculated for $C_{21}H_{17}N_4O$ 341.1397; found 341.1404 [M + H][+].

***N,N*-Dimethyl-1,3,7-triazapyren-6,8-diamine** (**3f**). Orange-colored solid (86 mg, 65%), mp 239-240 °C (from EtOH). ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.36 (s, 6H, NMe$_2$), 7.27 (d, *J* 9.2 Hz, 1H, H-4), 7.35 (d, *J* 9.0 Hz, 1H, H-10), 7.64 (br. s, 2H, NH$_2$), 8.44 (d, *J* 9.2 Hz, 1H, H-5), 8.55 (d, *J* 9.0 Hz, 1H, H-9), 8.99 (s, 1H, H-2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 42.5, 103.2, 103.7, 115.9, 117.5, 118.6, 131.1, 132.0, 133.8, 154.8, 155.2, 156.5, 157.4, 159.7. IR: 3315, 3151, 1663, 1643, 1593, 1574 cm^{-1}. HRMS (ESI): calculated for C$_{15}$H$_{14}$N$_5$ 264.1244; found 264.1244 [M + H]$^+$.

2-Methyl-1,3,7-triazapyren-6-amine (**3g**). Pale brown solid (6 mg, 5%), subl. p. 266 °C (from EtOH), ref.[21] 266 °C.

(1,1-Dimethylpentyl)-urea. Finely powdered urea (6 g, 0.1 mole) was added with stirring to concentrated H$_2$SO$_4$ (19.3 g, 0.198 mole, d = 1.84), cooled in an ice bath, at such a rate that the temperature remained between 20-25 °C. Then 2-methylhexan-2-ol (23.2 g, 0.2 mol) was added dropwise maintaining the mixture temperature within the same range. After the addition was completed the mixture was stirred for an additional 30 minutes, allowed to stand at rt overnight, and then poured with stirring onto cracked ice (~ 150 g). Without removal of the precipitate, the mixture was made alkaline to Congo red indicator by adding slowly with stirring a solution of NaOH (16 g in 75 mL of H$_2$O). The mixture was cooled with an ice bath to keep the temperature below 25 °C. The mixture was stirred in the ice bath until the temperature fell to about 15 °C, at which point the precipitate was filtered off and washed with cold H$_2$O (2 x 100 mL). The crude product was recrystallized from H$_2$O. White solid (7.2 g, 45%), mp 105–106 °C (from H$_2$O). ^{1}H NMR (400 MHz, DMSO-D$_6$): δ 0.88 (t, *J* 6.8 Hz, 3H, C*H$_3$*CH$_2$), 1.19-1.32 (m, 10H, C(C*H$_3$*)$_2$ and C*H$_2$*C*H$_2$*CH$_3$), 1.61 (br. t, *J* 8.0 Hz, 2H, C(CH$_3$)$_2$C*H$_2$*), 4.57 (br. s, 2H, NH$_2$), 4.94 (br. s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-D$_6$): δ 14.3, 23.3, 26.5, 27.6, 40.9, 52.8, 158.6. IR: 3456, 3356, 3213, 2953, 1653, 1600, 1555 cm^{-1}.HRMS (ESI): calculated for C$_8$H$_{19}$N$_2$O 159.1492; found 159.1494 [M + H]$^+$.

1-(*tert*-Butyl)-3-(1,3,7-triazapyren-6-yl)-urea (9a) and 7*H*-1,3,7-Triazapyren-6-one (10). The reaction vessel must be protected from the air moisture, but not from air oxygen. To a solution of the *tert*-butylurea (174 mg, 3 mmol) in anhydrous DMSO (5 mL) NaH (120 mg, 3 mmol, based on active ingredient) was added at rt. When hydrogen bubbling ceased, 1,3,7-triazapyrene (**1a**) (103 mg, 0.5 mmol) was added. The mixture was stirred at rt for 7 h, poured onto crushed ice (50 g), and allowed to warm to rt. The precipitate obtained was filtered off, washed with cold H$_2$O, and dried. The dry product was recrystallized from CH$_2$Cl$_2$ (~ 50 mL) to form 1-(*tert*-butyl)-3-(1,3,7-triazapyren-6-yl)urea (**9a**). Pure 7*H*-1,3,7-triazapyren-6-one(**10**) was obtained by extracting the aqueous filtrate with 1-butanol (3x3 mL) and distilling off the solvent under reduced pressure followed by recrystallization from EtOH.

1-(*tert*-Butyl)-3-(1,3,7-triazapyren-6-yl)-urea (9a). Yellow solid (73 mg, 46%), mp 235-236 °C (from CH$_2$Cl$_2$). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.46 (s, 9H, C(C*H$_3$*)$_3$), 8.00 (d, *J* 9.2 Hz, 1H, H-4), 8.18 (d, *J* 9.3 Hz, 1H, H-10), 8.69 (d, *J* 9.2 Hz, 1H, H-5), 9.32 (d, *J* 9.3 Hz, 1H, H-9), 9.45

(s, 1H, H-8), 9.71 (s, 1H, H-2), 9.86 (br. s, 1H, N*H*Bu^t), 10.08 (br. s, 1H, N*H*Ar) ppm.* IR: 3224, 3185, 3134, 1675, 1557, 1507 cm^{-1}. HRMS (ESI): calculated for $C_{18}H_{18}N_5O$ 320.1511; found 320.1513 [M + H]$^+$.

7*H*-1,3,7-Triazapyren-6-one (10). Yellow solid (44 mg, 40%), subl.p. 285-286 °C (from EtOH), ref[21] 286 °C.

1-(1,1-Dimethyl-pentyl)-3-(1,3,7-triazapyren-6-yl)-urea (9b). The reaction vessel must be protected from the air moisture, but not from air oxygen. To a solution of the (1,1-dimethyl-pentyl)urea (474 mg, 3 mmol) in anhydrous DMSO (5 mL), NaH (120 mg, 3 mmol, based on active ingredient) was added at rt. When hydrogen bubbling ceased, 1,3,7-triazapyrene (**1a**) (103 mg, 0.5 mmol) was added. The mixture was stirred vigorously at rt for 2 h. Then H_2O (20 mL) was added to the reaction mixture. The precipitate obtained was filtered off, washed with H_2O and dried. Pale brown solid (170 mg, 94%), mp 218-219 °C (from EtOH). ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.93 (t, *J* 6.9 Hz, 3H, CH$_2$CH$_2$C*H$_3$*), 1.34-1.39 (m, 4H, C*H$_2$*C*H$_2$*CH$_3$), 1.43 (s, 6H, C(C*H$_3$*)$_2$), 1.74-1.79 (m, 2H, C*H$_2$*CH$_2$CH$_2$CH$_3$), 8.00 (d, *J* 9.2 Hz, 1H, H-4), 8.18 (d, *J* 9.4 Hz, 1H, H-10), 8.70 (d, *J* 9.2 Hz, 1H, H-5), 9.32 (d, *J* 9.4 Hz, 1H, H-9), 9.44 (s, 1H, H-8), 9.71 (s, 1H, H-2), 9.88 (br. s, 1H, N*H*Alk), 10.01 (br. s, 1H, N*H*Ar). ^{13}C NMR (100 MHz, DMSO-d_6): δ 14.4, 23.4, 26.7, 27.4, 41.1, 53.9, 111.2, 116.3, 119.4, 125.8, 127.5, 128.4, 130.4, 134.7, 145.5, 150.7, 154.3, 154.7, 156.5, 158.3. IR: 3227, 3178, 3137, 1675, 1631, 1600, 1555 cm^{-1}. HRMS (ESI): calculated for $C_{21}H_{24}N_5O$ 362.1975, found 362.1985 [M + H]$^+$.

7*H*-1,3,7-Triazapyren-6-one (10). To a solution of the (1,1-dimethylpentyl)urea (474 mg, 3 mmol) in anhydrous DMSO (5 mL), NaH (120 mg, 3 mmol, based on active ingredient) was added at rt. When hydrogen bubbling ceased, the temperature was increased up to 70-75 °C and 1,3,7-triazapyrene (**1a**) (103 mg, 0.5 mmol) was added. The mixture was stirred vigorously at this temperature for 2 h. After cooling to rt H_2O (50 mL) was added to the reaction mixture. The product (**10**) was obtained by extracting the aqueous solution with 1-butanol (3x3 mL) and distilling off the solvent under reduced pressure. Yellow solid (80 mg, 72%), subl. p. 285-286 °C (from EtOH), ref.[21] 286 °C.

Conversion of 1-(*tert*-Butyl)-3-(1,3,7-triazapyren-6-yl)-urea (9a) into 1,3,7-Triazapyren-6-amine (3a). A solution of 1-(*tert*-butyl)-3-(1,3,7-triazapyren-6-yl)-urea (159.5 mg, 5 mmol) in xylene (20 mL) was refluxed for 1 h. After cooling to rt the precipitate of **3a** was filtered off, washed with H_2O and dried. 1,3,7-Triazapyren-6-amine (**3a**) was obtained as brown solid (100 mg, 91%), subl. p. 250 °C (from EtOH), ref.[21] 250 °C.

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*^{13}C NMR spectrum of compound **10a** could not be recorded due to insufficient solubility.

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