Synthesis and Reactions of (1*E*,2*Z*)-2-*N*,*N*-Dialkylhydrazono-2-phenylethanal *N*,*N*-Dimethylhydrazones

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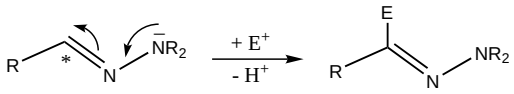
Abstract: (1*E*,2*Z*)-2-*N*,*N*-Dialkylhydrazono-2-phenylethanal *N*,*N*-dimethylhydrazones **3a–e** were synthesised by the reaction of 1,4,5-triazapentadienium salts **2** with *N*,*N*-dimethylhydrazine. The compounds **3a** and **3d** did not react with tosyl isocyanate in an electrophilic substitution reaction at the azomethine C-1 as aza-enamines, but they reacted at room temperature in benzene in a 1,4-dipolar cycloaddition to yield 1,3,5-triazinan-2,4-diones **5a** and **5d**, whereas at 70 °C octahydroimidazoimidazol-2,5-dione **6a** was formed via criss-cross addition reaction. With dimethyl sulfate in DMF, **3a** was transformed into the trimethylhydrazonium salts **7a** and **8a**, isolated as co-crystallised perchlorates (molar ratio 1:1).

Key words: aza-enamines, heterocycles, hydrazonium salts, 1,4-dipolar cycloaddition, criss-cross addition reaction

Aldehyde hydrazones can be considered as aza-enamines.[1a,d,f] Like enamines[2] they are attacked from electrophilic reagents at their nucleophilic center, i.e. the azomethine C-atom (*) (Scheme 1).



* : Azomethine-C-atom

R: alkyl, aryl
NR_2: dimethylamino
pyrrolidino

Scheme 1

For example, they react with the Vilsmeier–Haack reagent to yield hydrazones of 2-oxoethanals (E = CHO),[1a–c,1h] with the Mannich reagent to give hydrazones of aminomethyl ketones (E = $CH_2NR'_2$),[1d] with tosyl isocyanate to form tosyl amides (E = CONHTs)[1b,1d–g] etc.[3–5] As a prerequisite for a successful reaction the aldehyde hydrazones need–in analogy to enamines– a terminal amino group which is a good electron donor, like the dimethylamino or the pyrrolidino group.[2]

In our study presented here, it was our initial question whether 2-*N*,*N*-dialkylhydrazono-2-phenylethanal *N*,*N*-dimethylhydrazones **3** (Scheme 2) would also behave as aza-enamines being liable to electrophilic reaction at C-1.

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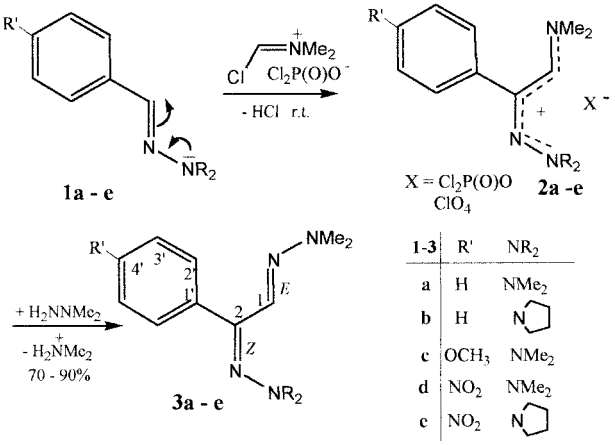
We found that compounds **3** bearing only alkyl groups at the terminal N-atom have not been described in the literature so far. Here we report on the synthesis of bishydrazones **3** and their reactions with electrophilic reagents like tosyl isocyanate and dimethyl sulfate.

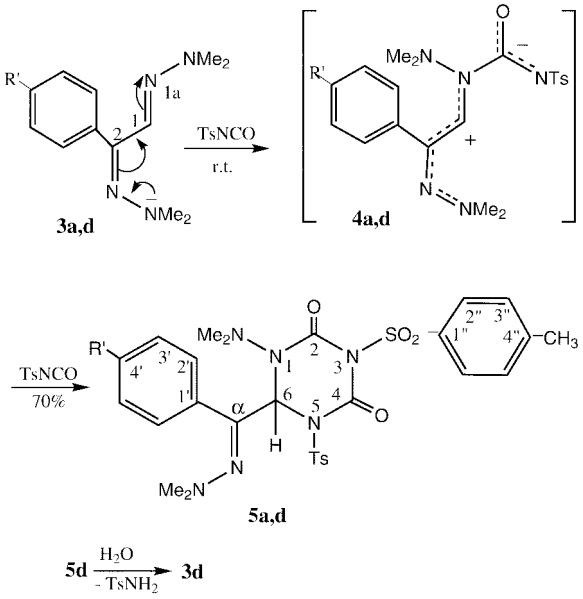


Scheme 2

As starting material for the synthesis of compounds **3**, 1,4,5-triaza-pentadienium salts **2** were used which were prepared by reacting benzaldehyde *N*,*N*-dialkylhydrazones **1** with the Vilsmeier–Haack reagent (Scheme 2). These 1,4,5-triazapentadienium salts **2** easily reacted at room temperature with *N*,*N*-dimethylhydrazine (DMH) to yield compounds **3.** The starting materials **2a**,**b** and **d** were reacted as perchlorates (X = ClO_4)[1b,c] in an apolar solvent. Isolation of **2c** and **2e** as perchlorates failed.[1c] In these cases dimethylhydrazine was added in excess to the crude reaction mixture of **2c** and **2e** [X = $Cl_2P(O)O$] and the formed **3c** and **3e** were isolated as hydroperchlorates. Thus, we not only synthesised hydrazones with the same alkyl groups at the terminal amino groups **3a**,**c**,**d** but also those with different alkyl groups **3b** and **e**. Characteristic for the compounds **3** are the chemical shifts of their azomethine protons (position 1) in the ^{1}H NMR spectra being in the range of 7.14–7.47 ppm.

The reaction of **3a** with tosyl isocyanate proceeded in a two-step mechanism (Scheme 3). First step was the electrophilic attack at the azomethine N-atom in the 1a-position of **3** forming the intermediate 1,4-dipole **4** which subsequently reacted with a second equivalent of tosyl isocyanate in a 1,4-dipolar cycloaddition[6] to give the

1,3,5-triazinan-2,4-diones **5a**. The ^{1}H NMR signal at δ = 6.25 for the proton in position 6 proved the attack of the isocyanate at position 1a of the compound **3a**. An additional argument for this structure was provided by the signal at δ = 76.6 in the ^{13}C NMR spectrum assigned to C-6 of **5a**. These signals are characteristic for such 1,3,5-triazinan-2,4-diones **5.**[1e]



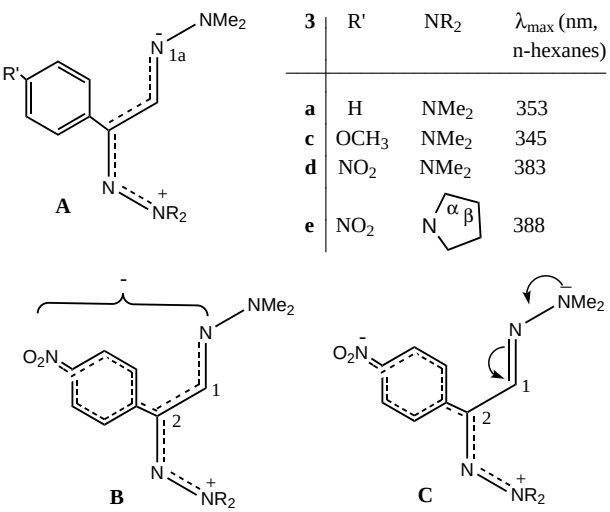
Scheme 3

As a result, the bishydrazone **3a** did not react – as expected – like an aza-enamine in a electrophilic substitution reaction at azomethine C-1 but in an addition reaction at the N-atom 1a.

By introducing a nitro group in position 4′ of the aromatic core we tried to diminish the electron density at N-atom 1a (Figure 1, structure **A**) by decoupling the twin aza-enamine (diene) system according to Figure 1, resonance structures **B** and **C**. The influence of the nitro group can be deduced from the λ_{max} values shown in Figure 1. A red shift of 30–40 nm was observed on comparing **3a** and **3c** with **3d** and **3e** (see also Ref.[7]).

Corresponding with this fact, the angle C(7)–N(6)–C(8) of the dimethylamino group 1b in the crystal of **3d** (Figure 2) amounts to 122.0° and the bond distances of N(6)–N(5) and N(5)–C(4) amount to 1.334 and 1.285 Å indicating a π-electron delocalisation favouring the resonance structure C in Figure 1.

Because of these results, an electrophilic substitution reaction at the azomethine C-1 according to the aza-enamine concept could be expected. Nevertheless, the nitro compound **3d** reacted with the tosyl isocyanate in the same manner as **3a** and did not behave as shown in Figure 1, structure **C**; i.e. **3d** was not attacked at the azomethine C-1 under substitution of the proton but an addition reaction occurred at the N-atom 1a forming compound **5d**. Thus, the decoupling of the twin aza-enamine was not sufficient.



3	R'	NR_2	λ_{max} (nm, n-hexanes)
a	H	NMe_2	353
c	OCH_3	NMe_2	345
d	NO_2	NMe_2	383
e	NO_2	N α β	388

Figure 1 Dipolar resonance structures of compounds **3** and their UV absorptions

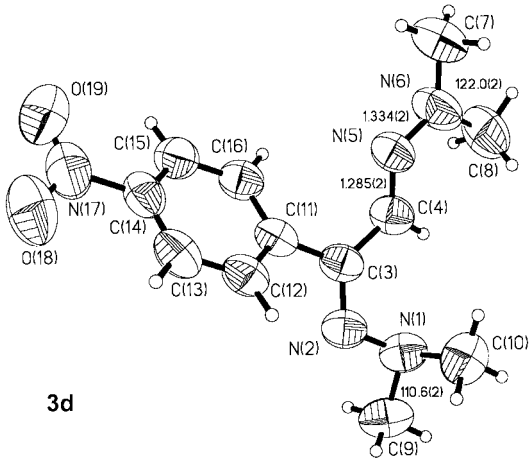
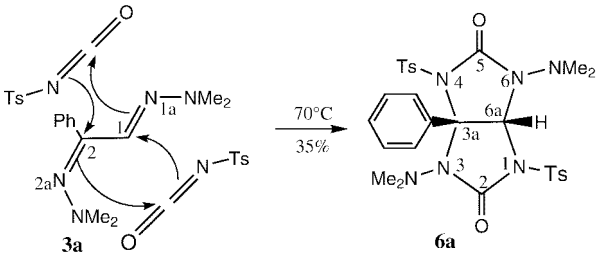


Figure 2 Crystal structure of the compound (1*E*,2*Z*)-**3d**. Selected bond distances (Å): N(6)–N(5) = 1.334, N(5)–C(4) = 1.285, C(4)–C(3) = 1.453, C(3)–N(2) = 1.292, N(2)–N(1) = 1.426. Selected bond angels: C(7)–N(6)–C(8) = 122.0°, C(9)–N(1)–C(10) = 110.6°. The compounds **3e** and **3b·HClO$_4$** show similar values for the distances N(6)–N(5) and N(5)–C(4) and the angle C(7)–N(6)–C(8).

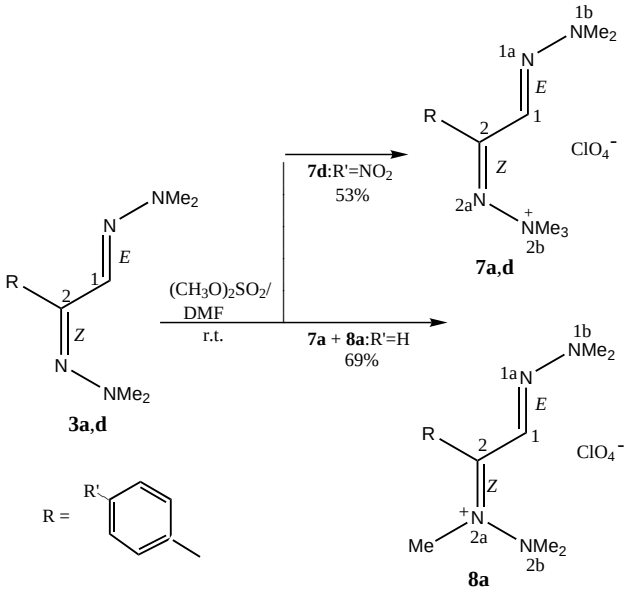
The structure of **5d** was proved by the signal at 6.28 ppm in the ^{1}H NMR spectrum for the proton in position 6 and its ^{13}C NMR signal at 76.5 ppm for C-6. Compound **5d** is sensitive towards hydrolysis. It gradually decomposed at room temperature and faster at 70 °C in aqueous MeCN forming back the red coloured **3d** and tosyl amide (Scheme 3). In refluxing benzene, however, **3a** reacted with tosyl isocyanate in a [2+3] criss-cross addition reaction to yield the imidazoimidazol-2,5-dione **6a**[8] (Scheme 4).



Scheme 4

The ^{1}H NMR spectrum shows signals at 77.2 and 82.5 ppm for C-6a and -3a and a singlet at 5.27 ppm for the proton at C-6a. Furthermore, the structure of **6a** was determined by an X-ray crystallographic analysis. In contrast to the reaction at room temperature, discussed above, at 70 °C **3a** was attacked by tosyl isocyanate on both sides of the molecule at the azomethine N-atoms in 1a and in 2a position. A formation of the corresponding compound **6d** from **3d** under the same reaction conditions could not be detected.

Finally, we treated the bishydrazones **3a** and **3d** with dimethyl sulfate in DMF at room temperature, aiming to formylate these compounds at the azomethine C-1 by using this soft formylation reagent.[9] Instead of being formylated, compound **3a** was methylated at room temperature at two positions, either at N-2a or at N-2b resulting after addition of $NaClO_4$ in a mixture of compounds **7a**[10] and **8a** (Scheme 5).



Scheme 5

Recrystallisation from MeOH led to a co-crystallised product which contained **7a** and **8a** in a molar ratio 1:1. This fact was confirmed by the ^{1}H NMR spectrum which indicated all signals of compounds **7a** and **8a** well separated and in a molar ratio of 1:1. A further evidence for structure **8a** came from the fact that the methyl group at N-2a caused a rotational hindrance to the neighbouring dimethylamino group indicated by splitting in two signals at 3.33 and 3.25 ppm. The decisive proof of the positions of the introduced methyl groups resulted from the X-ray crystallographic analysis, confirming the methylation of N-atoms 2a or 2b. The 1:1 composition of the co-crystallisate was verified by X-ray analysis, showing **7a** and **8a** as two independent molecules of the same configuration; the substituents at the double bonds C-1/N-1a are *E*-configured, those at the double bonds C-2/N-2a are *Z*-configured. The same configurations were established for compound **7d** as well as **3b**·$\mathbf{HClO_4}$ and **3d** (Table 1). Alkylation of **3d** exclusively resulted in quaternisation at the terminal amino group 2b to **7d**. Pure **7a** could be isolated from the methanolic mother liquor of the recrystallisation. As a result, also with the reagent $(MeO)_2SO_2$/DMF a formylation reaction at the C-1 did not happen.

The preference for the electrophilic attack at N-2a and N-2b in comparison to N-1a and N-1b in compound **8a** and at N-2b in **7a**,**d** (Scheme 5) may be caused by the thermodynamic control of the alkylation reaction. The alkylation at position 2b could be attributed to the lone pair of the amino group 2b in **3d** [Figure 2, angle C(9)–N(1)–C(10): 110.6°] in contrast to the sp^2-hybridisation of the amino group 1b [Figure 2, angle C(7)–N(6)–C(8): 122.0°]. Also in the compound **3b**·$\mathbf{HClO_4}$ the nitrogen atom of the pyrrolidino group in position 2b is protonated.

The question why tosyl isocyanate attacked the azomethine nitrogen in 1a position can not be answered distinctly. Presumably, steric reasons favour the attack of tosyl isocyanate at the N-1a being in the γ-position with respect to the aromatic core.

The attack of the isocyanate at the N-atoms 1a and 2a and of the dimethyl sulfate/DMF at the atoms 2a and 2b led to the stable final products **5**, **6a** as well as **7** and **8**, respectively (Schemes 3– 5). The attack of electrophilic agents such as trifluoroacetophenone , trifluoroacetic anhydride, the Vilsmeier or the Mannich reagent etc. to the N-atoms of the compounds **3** can not lead to stable products. The question is not answered up to now, whether the attack in this cases alternatively would take place at the azomethine C-1 forming stable final products in an electrophilic substitution reaction corresponding the aza-enamine concept.

The NMR spectra (instrument DMX 400 (Bruker)) were recorded at 300, 400, 500 MHz and 75, 100, 125, respectively. For calibration the solvent signals: $CDCl_3$ 7.23 ppm (^{1}H) and 77.0 ppm (^{13}C), CD_3CN 1.93 ppm (^{1}H) and 1.3 ppm (^{13}C) were used. Microcombustion analyses were performed by Elemental Analyzer 1110 CHNS, CE Instruments. Mass spectra were recorded in 'Liquid secondary Ion Mass Spectrometry-mode', spectrometer AUTOSPEC, firm Micromass. The yields were not optimised.

(1*E*,2*Z*)-2-*N*,*N*-Dimethylhydrazono-2-phenylethanal *N*,*N*-Dimethylhydrazone (3a)

Benzaldehyde *N*,*N*-dimethylhydrazone (**1a**;[1c,11] 7.0 g, 47 mmol) [prepared from benzaldehyde (10.6 g, 100 mmol), *N*,*N*-dimethylhydrazine (DMH, 6.6 g, 110 mmol) and AcOH (3 drops) in refluxing

Table 1 ^{1}H NMR Spectra of Compounds **3**, **5**–**8** and References to X-Ray Analyses Data

Product	^{1}H NMR (MeCN) δ, *J* (Hz)
3a	300 MHz: 7.54 (2 H, C-2′[a]), 7.46 (s, 1 H,C-1), 7.32 (2 H,C-3′), 7.35 (1 H,C-4′), 2.97 [s, 6 H, $N(CH_3)_2$, br[b]] 2.55 [s, 6 H, $N(CH_3)_2$, sharp)
3b·HClO$_4$[c]	7.32 (m, 5 H,C-2′,3′,4′), 7.14 (s, 1 H, C-1), 2.85 [m,[d] 4 H (α)], 2.77 [s, 6 H, $N(CH_3)_2$, br], 1.64 [m,[d] 4 H (β)]
3c	400 MHz: 7.53 (2 H, C-2′[e]), 7.47 (s, 1 H, C-1), 6.87 (2 H, C-3′), 3.79 (s, 3 H, OCH_3), 2.97 [s, 6 H, $N(CH_3)_2$, br[b]), 2.55 [s, 6 H, $N(CH_3)_2$, sharp]
3d[c]	300 MHz ($CDCl_3$): 8.20 (2 H, C-3′[e]), 7.80 (2 H, C-2′), 7.43 (s, 1 H, C-1), 3.08 [s, 6 H, $N(CH_3)_2$, br[b]], 2.71 [s, 6 H, $N(CH_3)_2$, sharp]
3e[c]	400 MHz: 8.13 (2 H, C-3′[e]), 7.83 (2 H, C-2′), 7.18 (s, 1 H, C-1), 3.28 [m,[d] 4 H (α)], 2.96 [s, 6 H, $N(CH_3)_2$, br[b]), 1.85 [m [d],4 H (β)]
5a	400 MHz: 6.25 (s, 1 H, C-6), 7.50–7.34 (m, 9 H, C-2′,3′,4′,C-3″), 8.06 (2 H,C-2′″[e]), 7.83 (2 H, C-2″), 2.46 (CH_3, C-4″), 2.45 (CH_3, C-4′″), 2.33 [very br, 6 H, $N(CH_3)_2$], 2.23 [s, 6 H, $N(CH_3)_2$ at N-1]
5d	400 MHz ($CDCl_3$): 6.28 (s, 1 H, C-6), 8.18 (2 H, C-3′[e]), 7.52 (2 H, C-2′), 8.13 (2 H, C-2″), 7.80 (2 H, C-2′″), 7.25 (2 H, C-3′″), 7.34 (2 H, C-3″), 2.37 [s, 6 H, $N(CH_3)_2$ at N-1], 2.48 [6 H, $N(CH_3)_2$, br], 2.42 (CH_3, C-4″), 2.40 (CH_3, C-4′″)
6a	500 MHz: 5.27 (s, 1 H, C-6a), 7.45 (2 H, C-2′[a]), 7.52 (2 H, C-3′), 7.52 (1 H, C-4′), 7.86 (2 H, C-2′″[e]), 7.78 (2 H, C-2″), 7.41 (2 H, C-3′″), 7.35 (2 H, C-3″), 2.93 (s, 3 H, NCH_3 at N-3), 2.50 (s, 3 H, NCH_3 at N-3), 2.52 [6 H, very br, $(CH_3)_2$ at N-6], 2.44 (CH_3, C-4″), 2.43 (CH_3, C-4′″)
7d[c]	400 MHz: 6.92 (s, 1 H, C-1), 8.23 (2 H, C-3′[e]), 7.66 (2 H, C-2′), 3.56 [s, $N(CH_3)_3$, 9 H), 3.22 [s, 6 H, $N(CH_3)_2$, br[b]]
7a[c,f]	400 MHz: 6.91 (s, 1 H, C-1), 7.48 (2 H, C-2′[a]), 7.40 (2 H, C-3′), 7.47 (1 H, C-4′), 3.35 [s, $N(CH_3)_3$, 9 H], 3.21 [6 H, $N(CH_3)_2$, br[b], N-1b]
8a[c,f]	400 MHz: 7.79 (s, 1 H, C-1), 7.33 (2 H, C-2′[a]), 7.44 (2 H, C-3′), 7.58 (1 H, C-4′), 3.33[g] (s, 3 H, CH_3 at N-2b), 3.25[g] (s, 3 H, CH_3 at N-2b), 3.07 (s, 3 H, CH_3 at N-2a), 2.73 [s, 6 H, $N(CH_3)_2$ at N-1b]

[a] The assignment of the phenyl groups in the ^{1}H NMR spectra of **3a**, **6a** and of the crystals consisting of **7a** and **8a** resulted from computer simulation.

[b] The hindrance of the rotation of the dimethylamino groups of compounds **3a**,**b**·**HClO$_4$**,**c**,**d**,**e**,**7a** and **7d** in the segment $Me_2NN{=}CH$(C-1) causes strong broadening of the signals in the ^{1}H NMR-spectra.

[c] Structure was confirmed by a X-ray crystallographic analysis; complete data were deposited at the Cambridge Crystallographic Data Center under the following registered CCDC-numbers. **3b**·**HClO$_4$** CCDC 171743; **3d**: CCDC 171743; **3e**: CCDC 210614; **6a**: CCDC 171740; **7a**: CCDC 171741 and 171742; **7d**: CCDC 171744; **8a**: CCDC 171741. Copies can be obtained from CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [e-mail: deposit@ccdc.cam.ac.uk].

[d] The signals of the pyrrolidino groups of **3b** and **3e** have the design of AA′A″A′″BB′B″B′″-spectra.

[e] The signals of the ^{1}H NMR spectra of the 4′-substituted phenyl groups (4′-nitrophenyl-, 4′-methoxyphenyl- and the tosyl groups, respectively) have the known feature of an AA′BB′-spin system.

[f] Compounds **7a** and **8a** were formed as co-crystallisate, the ^{1}H NMR spectrum showed all signals of both compounds well separated, well assignable and in a molar ratio 1:1.

[g] The existence of both signals at δ = 3.33 and 3.25 assigned to the methyl groups in position 2b of **8a** indicated the inhibition of their rotation.

anhyd EtOH (10 mL) for 2.5 h, yield: 14.33 g (97%)] was dissolved in anhyd DMF (5 mL) and Vilsmeier–Haack reagent (Vilsm. rg.) (28.2 g, 94 mmol) was added slowly under ice cooling [1 mol Vilsm. rg. = 300 g from $POCl_3$ (150 g, 1 mol) + DMF (150 g, 2 mol)]. After 2 h, the mixture was poured onto ice (50 g) and a solution of $NaClO_4$ (20 g, 143 mmol) in H_2O (15 mL) was added. The precipitate **2a** (X = ClO_4, mp 118–127 °C)[1b,c] was separated and washed with EtOH (10 mL). To a stirred suspension of **2a** in EtOH (40 mL) was added *N*,*N*-dimethylhydrazine (DMH) (3.18 g, 53 mmol) at r.t. After 1 h, EtOH was evaporated, the residue was dissolved in Et_2O and the solution was washed with H_2O until neutral; yield: 7.59 g (74%); yellow oil; crude product pure enough for further reactions. Additional purification was carried out as follows: A sample of crude **3a** was dissolved in a small amount of DMF and dil. aq $HClO_4$ was added. The precipitate [mp 137–140 °C (MeOH) beige coloured crystals] was suspended in Et_2O and transformed into the free base by shaking with dil. aq NaOH solution; pure **3a**: mp 33–36 °C; yellow crystals.

^{13}C NMR (75.9 MHz, MeCN): δ = 162.0 (C-2), 139.0 (C-1′), 130.3 (C-2′), 129.3 (C-4′), 128.2 (C-3′), 125.1 (C-1), 48.0 (CH_3), 42.4 (CH_3).

MS: *m*/*z* = 219 (M + 1).

Anal. Calcd for $C_{12}H_{18}N_4$ (218.30): C, 66.02; H, 8.31; N, 25.67: Found: C, 66.25; H, 8.36; N, 25.48.

(1*E*,2*Z*)-2-*N*,*N*-Tetramethylenehydrazono-2-phenylethanal *N*,*N*-Dimethylhydrazone Perchlorate 3b·HClO$_4$

Compound **2b** [X = ClO_4, mp 143–148 °C;[1c] 2.2 g, 6.67 mmol, synthesised in analogy to **2a** (X = ClO_4)] was suspended in benzene and DMH (0.627 g, 10.5 mmol) was added at r.t. After 1 h, the solution was washed with H_2O until neutral and dried ($CaCl_2$). The crude **3b** was purified by filtration of its benzene solution through a layer of silica gel (2 cm high, ∅ 1 cm); yield: 1.4 g (86%); mp 76–78.5 °C; yellow solid. A sample in Et_2O was treated with $HClO_4$

giving **3b·HClO$_4$**; mp 108.5–112 °C (MeOH); yellow crystals, decomposed slowly at r.t.

(1*E*,2*Z*)-2-*N*,*N*-Dimethylhydrazono 2-(4-methoxyphenyl)ethanal *N*,*N*-Dimethylhydrazone (3c)

Vilsm. rg. (3 g, 10 mmol) was added to an ice-cooled solution of **1c**[1c] [(0.89 g, 5 mmol), prepared from 4-methoxybenzaldehyde (4 g, 30 mmol), DMH (2.16 g, 36 mmol), AcOH (2 drops) in anhyd refluxing EtOH for 2 h; yield: 4.88 g (91%)] in DMF (1 mL). After 20 h, DMH was added dropwise to this cooled reaction mixture until pH 9 was reached, the solution was mixed with Et_2O, washed with H_2O till neutral and dried ($CaCl_2$). The crude **3c** was an yellow sirup and was purified by treatment with $HClO_4$ in Et_2O to form a bishydrazonium perchlorate that was recrystallised by dissolving in a small amount of MeOH followed by addition of hot EtOAc up to the beginning of the crystallisation; mp 173–175 °C; yellow crystals (1.49 g). The free base **3c** was obtained by shaking the hydroperchlorate in Et_2O with aq 25% NaOH solution and the organic layer was afterwards washed with H_2O until neutral; yield: 0.855 g (69%); oil.

Anal. Calcd for $C_{13}H_{20}N_4O$ (248.32): C, 62.87; H, 8.12; N, 22.56: Found: C, 62.79; H, 7.95; N, 21.43.

(1*E*,2*Z*)-2-*N*,*N*-Dimethylhydrazono-2-(4-nitrophenyl)ethanal *N*,*N*-Dimethylhydrazone (3d)

DMH (0.3 g, 5 mmol) was slowly added to a suspension of **2d** [X = ClO_4, mp 130–132 °C;[1b,c] 1.462 g, 4.19 mmol, synthesised in analogy to **2a** (X = ClO_4)] in benzene (7 mL). After 1 h, the black coloured solution was washed with H_2O, the organic solution was dried ($CaCl_2$) and the solvent was evaporated. Compound **3d** was a dark-red to black coloured sirup and did not crystallise. It was treated in DMF (3 mL) with $HClO_4$ (15 mmol in 5 mL H_2O). The yellow bishydrazonium perchlorate [mp 167–170 °C (MeOH)] was washed with H_2O, stirred with aq 25% NaOH solution and Et_2O. The organic layer was washed with H_2O, dried and the solvent was removed; yield (crude): 1.016 g (92%); mp 74.0–75.5 °C (hexanes); red coloured prisms.

Anal. Calcd for $C_{12}H_{17}N_5O_2$ (263.30): C, 54.74; H, 6.51; N, 26.60: Found: C, 54.79; H, 6.43; N, 26.43.

(1*E*,2*Z*)-2-*N*,*N*-Tetramethylenhydrazone-2-(4-nitrophenyl)-ethanal *N*,*N*-Dimethylhydrazone (3e)

Vilsm. rg. (0.45 g, 1.5 mmol) was added to an ice-cooled solution of **1e**[1d] (0.274 g, 1.25 mmol) in DMF (1 mL). After 1 h, DMH was added to this cooled reaction mixture until pH 9 was reached. The mixture was then stirred for 1 h, Et_2O was added and the Et_2O layer was washed with H_2O until neutral. Removal of Et_2O gave crude **3e** as a black resinous mass, which did not crystallise. It was treated in DMF with dil. aq $HClO_4$ to give a bishydrazonium perchlorate as a sirup, that crystallised overnight to a brown product. The free base **3e** was obtained by shaking the hydroperchlorate in Et_2O with aq 25% NaOH solution and isolated in the usual manner; yield (crude): 0.114 g (32%); mp 100.0–101.5 °C (heptanes); red coloured prisms.

Anal. Calcd for $C_{14}H_{19}N_5O_2$ (289.33): C, 58.11; H, 6.62; N, 24.21. Found: C, 58.31; H, 6.56; N, 23.82.

1-Dimethylamino-6-(α-*N*,*N*-dimethylhydrazonobenzyl)-3,5-ditosyl-1,3,5-triazinan-2,4-dione (5a)

Tosyl isocyanate (0.434 g, 2.2 mmol) was added to a solution of **3a** (0.218 g, 1 mmol) in benzene (2 mL) cooled to 5 °C. The mixture was kept at r.t. for 2 h and thereafter the solvent was removed in a rotary evaporator. To the residue MeOH was added to crystallise **5a**, which was analytically pure; yield: 0.459 g (75%); mp 132–134 °C. The melted product became solid again above 134 °C and was transformed into **6a.** A sample of **5a** recrystallised from AcOH also gave **6a**; mp 251–253 °C.

^{13}C NMR (400 MHz, $CDCl_3$): δ = 76.6 (C-6), 147.1, 145.9 (C-2,4), 134.0 (C-α), 125.5 (C-1′), 128.8 (C-2′), 128.8 (C-3′), 129.1 (C-4′), 135.5, 134.1 (C-1″), 129.7, 129.5 (C-2″), 129.4, 129.3 (C-3″), 145.4, 145.4 (C-4″), 46.3 (NCH_3 at N-1), 43.4 (NCH_3), 21.7, 21.6 (CH_3 at C-4″).

MS: *m*/*z* = 613 (M + 1).

Anal. Calcd for $C_{28}H_{32}N_6O_6S_2$ (612.70): C, 54.88; H, 5.26; N, 13.72. Found: C, 54.87; H, 5.22; N, 13.70.

1-Dimethylamino-6-[α-(*N*,*N*-dimethylhydrazono)-4-nitrobenzyl]-3,5-ditosyl-1,3,5-triazinan-2,4-dione (5d)

Tosyl isocyanate (0.13 g, 0.66 mmol) was added to **3d** (0.079 g, 0.3 mmol) in benzene (1 mL) and the mixture was kept for 5 d at r.t. Thereafter the solvent was evaporated and MeOH was added to the residue, the crystals obtained were washed with MeOH and filtered; yield (crude): 0.135 g (67%); mp 130–136 °C (EtOAc); yellow needles.

^{13}C NMR (400 MHz, $CDCl_3$): 76.5 (C-6), 146.9, 147.7 (C-2,4), 141.3 (C-α), 131.2 (C-1′),130.1 (C-2′), 123.7 (C-3′), 145.8 (C-4′), 135.3, 134.1 (C-1″), 129.6, 129.4 (C-2″), 129.3, 129.3 (C-3″), 145.7, 145.6 (C-4″), 46.7 (NCH_3 at N-1), 43.6 (NCH_3), 21.8, 21.6 (CH_3 at C-4″). The NMR spectra had to be recorded at once after dissolving **5d** in $CDCl_3$ because of its decomposition.

Anlal. Calcd for $C_{28}H_{31}N_7O_8S_2$ (657.70): C, 51.13; H, 4.75; N, 14.91. Found: C, 51.49; H, 4.62; N, 14.56.

Hydrolysis of 5d to 3d

A solution of **5d** (6.57 g, 10 mmol) in MeCN (20 mL) and H_2O (1 mL) was warmed to 70 °C. The compound dissolved under gas formation. The red coloured solution was stirred further for 20 min and the solvent was evaporated. Compound **3d** was separated from tosyl amide (mp 135–137 °C) by repeated extraction with cyclohexane (total amount 120 mL). The crude **3d**, after removal of the solvent, was dissolved in a few drops of warm EtOAc. Addition of warm heptanes (40 mL) to this solution allowed **3d** to crystallise slowly; yield: 2 g (76%); mp 73–74 °C.

3,6-Bis(dimethylamino)-3a-phenyl-1,4-ditosyloctahydroimidazo[4,5*d*]imidazol-2,5-dione (6a)

A solution of **3a** (0.218 g, 1 mmol) and tosyl isocyanate (0.434 g, 2.2 mmol) in benzene (1.5 mL) was kept at 70 °C for 2 h and the residue obtained after removal of benzene was allowed to crystallise from MeOH; yield (crude): 0.214 g (35%); mp 252–253.5 °C (MeOH). The compounds **5a** and **6a** could be observed well separated by TLC in EtOAc–hexanes (1:2) (Merck, Kieselgel 60 plates).

^{13}C NMR (75.9 MHz): δ = 82.5 (C-3a), 77.2 (C-6a), 151.3, 150.8 (C-2,5), 136.7 (C-1′), 127.0 (C-2′), 129.1 (C-3′), 130.5 (C-4′), 137.9, 137.3 (C-1″), 130.3, 130.5 (C-2″), 130.1, 129.9 (C-3″), 146.6, 146.5 (C-4″), 45.1, 44.7 (NCH_3 at N-3, N-6), 41.5 (very broad), 21.60, 21.62 (CH_3 at C-4″).

MS: *m*/*z* = 613 (M + 1).

Anal. Calcd for $C_{28}H_{32}N_6O_6S_2$ (612.70): C 54.88; H, 5.26; N, 13.72: Found: C, 55.27; H, 5.00; N, 13.53.

(1*E*,2*Z*)-2-*N*,*N*,*N*-Trimethylhydrazonium-2-(4-nitrophenyl)-ethanal *N*,*N*-Dimethylhydrazone Perchlorate (7d)

Dimethyl sulfate (0.39 g, 3.1 mmol) in DMF (1 mL) was added to **3d** (0.263 g, 1 mmol) dissolved in DMF (0.5 mL). After 15 h, the solution was poured into H_2O (3 mL). The amorphous precipitate was extracted with Et_2O and aq 50% $NaClO_4$ (1 mL) was added; yield: 0.20 g (53%); mp 192–195 °C (dec.) (MeOH); small yellow-brown staffs.

Anal. Calcd for $C_{13}H_{20}ClN_5O_6$ (377.79): C, 41.33; H, 5.34; N, 18.54. Found: C, 41.14; H, 5.25; N, 18.27.

Mixture of (1*E*,2*Z*)-2-*N*,*N*,*N*-Trimethylhydrazonium-2-phenylethanal *N*,*N*-Dimethylhydrazone Perchlorate (7a) and (1*E*,2*Z*)-2-*N*,*N*,*N*′-Trimethylhydrazonium-2-phenylethanal *N*,*N*-Dimethylhydrazone Perchlorate (8a)

Dimethyl sulfate (1.26 g, 10 mmol) in DMF (3 mL) was added to **3a** (0.8 g, 3.66 mmol) dissolved in DMF (1.5 mL). After 2 h at r.t., the solution was added to H_2O (10 mL). The amorphous precipitate was extracted with Et_2O and the solution was added to $NaClO_4$ (1.11 g, 7.9 mmol in 2 mL H_2O). A thick sirup was formed that became solid overnight. It was washed twice with EtOAc by stirring and filtered; yield (crude mixture): 0.843 g (69%); mp 150–153 °C (MeOH); yellowish coloured prisms.

Anal. Calcd for $C_{13}H_{21}ClN_4O_4$ (332.79): C, 46.92; H, 6.36; N, 16.84. Found: C, 46.82; H, 6.28; N, 16.68.

7a

Additionally a small amount of pure **7a** crystallised out. After separation of the co-crystallisate **7a** and **8a**, from the mother liquor of the recrystallisation, **7a** forms at first fine needles which changed after dilution of this solution with a small amount of H_2O to star like spears; mp 133–136 °C (MeOH).

X-Ray Crystal Analysis of 3d

Crystal Data: $C_{12}H_{17}N_5O_2$, triclinic, space group P-1, a = 9.5312(12) Å, b = 9.7709(12) Å, c = 9.9516(13) Å, α = 105.444(3)°, β = 103.348(2)°, γ = 117.754(3)°, V = 718.9(2) Å^3, Z = 2, Dc = 1.216 Mgm^{-3}, F(000) = 280, μ = 0.087 mm^{-1}, T = 293° K. Data Collection: A crystal of 0.905 × 0.55 × 0.35 mm was used to register 2495 independent intensities (Mo-Kα radiation, $2\theta_{max}$ 50°) on a Bruker AXS SMART diffractometer. Structure Refinement: The structure was refined anisotropically to R1 = 0.054. Hydrogen atoms were included using a riding model. X-ray data of the structures **7a**, **8a**, **3b**, **3d**, **3e**, **6a**, and **7d** were deposited at the Cambridge Crystallographic Data Center (CCDC) (see Table 1).

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