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Synthesis of 6- to 10-membered ring (*E*)-hydroxyiminohydroazaazoniabenzocycloalkenes derivative from cyclization of 2-nitromethylene-1-(ω-phenylalkyl)imidazolidine or 2-nitromethylene-1-(ω-phenylalkyl)hexahydropyrimidine in trifluoromethanesulfonic acid

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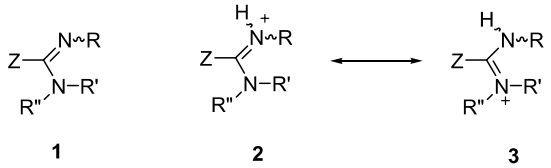
Abstract—In trifluoromethanesulfonic acid, 2-nitromethylene-1-(ω-phenylalkyl)imidazolidine or 2-nitromethylene-1-(ω-phenylalkyl)hexahydropyrimidine derivatives undergo an intramolecular cyclization to afford (*E*)-hydroxyiminohydroazaazoniabenzocycloalkenes, in their trifluoromethanesulfonate salt form. The reaction probably occurres via the formation of an electrophilic transient hydroxynitrilium ion (or *O*-protonated nitrile oxide). The yields are generally good, except for the higher-membered ring derivatives.

1. Introduction

Amidines have long been regarded as useful intermediates in the synthesis of heterocyclic compounds,[1] characteristic structural feature of many natural substances[2] and important pharmacophore in the active ingredients of drugs.[3,4] Because of these activities, substituted amidine-containing compounds have found frequent application in medicinal chemistry.[5,6]

From a structural point of view, amidines **1** have two nitrogen atoms in the 1,3-position of an allylic system (Fig. 1). This arrangement is particularly favorable for *n*-π heteroallylic nitrogen conjugation, which confers a highly basic character to the group. Because of this strong basic character, they are easily *N*-protonated to give resonance-stabilized amidinium cations with mesomeric formulas **2** and **3**[7] or they form strong interactions with proteins[8] and other biomolecules, particularly in regions bearing anionic and hydrogen bonding groups such as those found in DNA.[9] This kind of association plays a key role in their physiological activity[10] and explains why they are present in many drugs.



1 **2** **3**

Figure 1.

Numerous synthetic methods have been developed for the preparation of amidines, the first of which is the classical Pinner's reaction, dating back to the 1800's.[11] Amidine-containing compounds are generally prepared from nitriles, amides (with the help of PCl_5 or $Et_3O^+BF_4^-$ or P_2O_5) or thioamides involving highly acidic,[12] alkaline[13] or strongly reducing conditions.[14] For complex molecules with sensitive functions, a mild method starting from nitriles and *N*-acetylcysteine as a catalyst has also been described.[15]

Keywords: 2-Nitromethyleneimidazolidine derivatives; 2-Nitromethylene-hexahydropyrimidine derivatives; Trifluoromethanesulfonic acid; Cyclic hydroxyiminoamidines; Cyclization.
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In previous papers, we reported the behavior and reactivity of 1-arylamino-1-methylthio-2-nitroethene derivatives **4** (Fig. 2) and acyclic nitroketene *S*,*S*-acetals **5** in superacidic media in HF–SbF_5 and trifluoromethanesulfonic acid.[16,17]

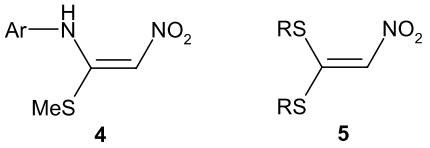


Figure 2.

In this paper, we present a new method for the synthesis of tricyclic (*E*)-hydroxyiminohydroazaazoniabenzocycloalkene derivatives in their triflate salt forms, starting from new cyclic nitroketene aminals, which were cyclized in trifluoromethanesulfonic acid.

2. Results and discussion

2.1. Starting material

Firstly, the appropriate linear monosubstituted diamines **9** and **10** bearing a tethered phenyl group were prepared, by reacting the corresponding 1-bromo-ω-phenyl derivatives **6** with excess 1,2-ethylenediamine **7** or 1,3-diaminopropane **8** (Scheme 1).

A potential synthon for the synthesis of nitroketene aminals derivatives is 1,1-bis(methylthio)-2-nitroethene **11**. In this compound, both methylthio groups are easily substituted by amino groups in mild conditions.[18,19] Reactions with aromatic[20] or non-aromatic amines[21] afford nitroketene *S*,*N*-acetals. Thus, nucleophilic substitution between one molar equivalent of diamine **9** or **10** and 1,1-bis(methylthio)-2-nitroethene **11** afforded the expected nitroketene aminals, either in the imidazolidine series **12** ($n=1$) or hexahydropyrimidine series **13** ($n=2$) with yields varying from 33 to 78% (Table 1).

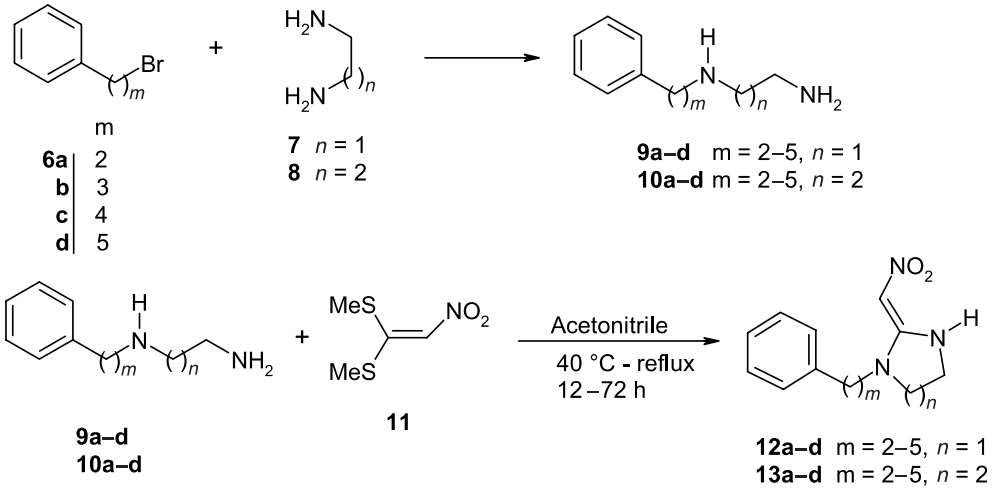
Compounds **12** and **13** were isolated by flash chromatography, followed by crystallization from a mixture of dichloromethane–petroleum ether. These compounds were characterized by NMR spectroscopy and HRMS.

For the imidazoline series **12**, a vinylic proton resonates in the range δ_H 6.48–6.52 ppm, the nitromethylene carbon $=CH–NO_2$ at δ_C 96.4–96.6 ppm and the $>C=C$ ethylene carbon at δ_C 159.0–159.3 ppm. In the hexahydropyrimidine series **13**, the observed chemical shifts are similar for the vinylic proton at δ_H 6.61–6.70 ppm and the nitromethylene carbon: δ_C 97.8–98.6 ppm but somewhat different for the ethylene carbon, which resonates at higher field due to a cycle effect: δ_C 153.8–154.5 ppm.[22]

In organic solvent solution, these compounds exist as sole isomers, as shown by a single set of signals in the ^{13}C NMR spectra. They are probably all (*E*)-isomers since this conformation allows the formation of an intramolecular hydrogen bond between the N–H and the $–NO_2$ groups, as previously reported for the 1-arylamino-1-methylthio-2-nitroethenes **4**.[20]

2.2. Reactions in trifluoromethanesulfonic acid

The reactions were carried out in trifluoromethanesulfonic acid at 60 °C under nitrogen atmosphere (Scheme 2).

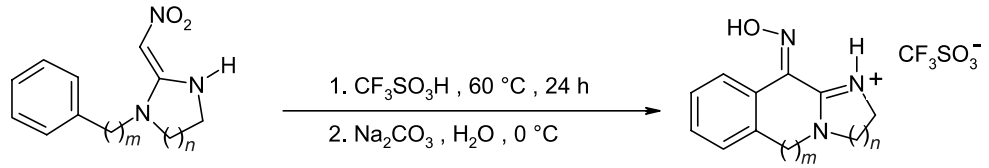


Scheme 1. Synthesis of imidazolidine and hexahydropyrimidine derivatives **12** and **13**.

Table 1. Yields of imidazolidine **12a–d** and hexahydropyrimidine **13a–d**

Starting diamine	**9a**	**9b**	**9c**	**9d**	**10a**	**10b**	**10c**	**10d**
Product	**12a**	**12b**	**12c**	**12d**	**13a**	**13b**	**13c**	**13d**
Yield (%)	78	62	33[a]	56	76	64	69	82

[a] With 25% of unreacted **11**.



12a–d m = 2-5, *n* = 1
13a–d m = 2-5, *n* = 2

14a–d m = 2-5, *n* = 1
15a–d m = 2-5, *n* = 2

Scheme 2. Preparation of cyclic hydroxyiminoamidine derivatives **14** and **15** from the corresponding imidazoline and hexahydropyrimidine **12** and **13**, respectively.

Table 2. Yields of triflate salts **14a–d** and **15a–d**

Starting compound	**12a**	**12b**	**12c**	**12d**	**13a**	**13b**	**13c**	**13d**
Triflate salt	**14a**	**14b**	**14c**	**14d**	**15a**	**15b**	**15c**	**15d**
Yield (%), isolated product	62	79	89	13	90	85	72	12

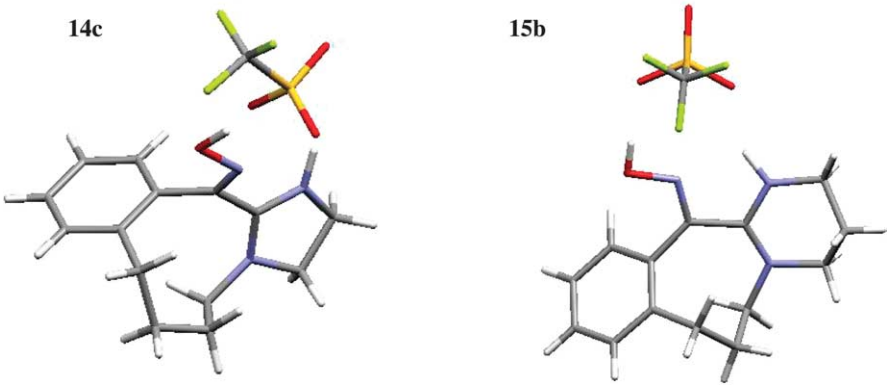


Figure 3. X-ray analysis of **14c** and **15b**.[23]

The molar ratio of trifluoromethanesulfonic acid/imidazolidine **12** or hexahydropyrimidine **13** molar was 50:1. At the end of the reaction, the acidic solution is poured into a mixture of ice (15 g) and anhydrous Na_2CO_3 (6 g) and the extraction is carried out promptly at approximately 0 °C with dichloromethane–methanol (95/5). The reactions were generally clean and the starting materials were fully transformed after 24 h reaction time, with yields varying from 12 to 90% (Table 2).

The structure of compounds **14** and **15** was determined by NMR and was corroborated by X-ray crystallographic analysis of **15b** and **15c** (Fig. 3).

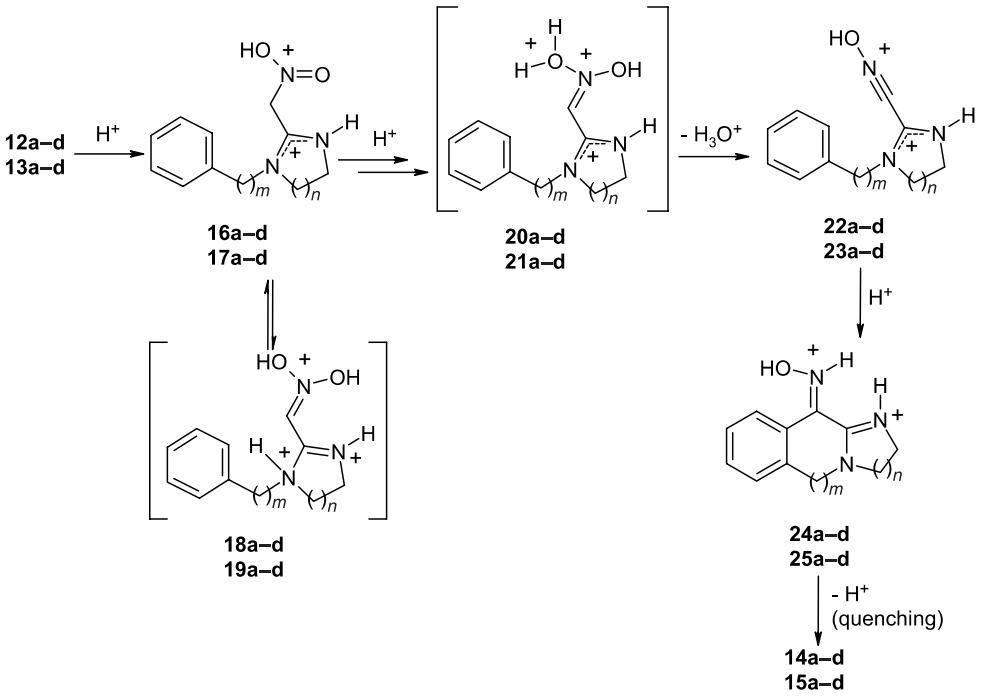
Crystal data for **14c** and **15d** were recorded at room temperature with a Nonius Kappa CDD difractometer equipped with a graphite monochromator and X-ray tube with a Mo anticathode (λ=0.71069 Å). The structure was solved using direct methods[24] and refined using least square calculation.[25]

The X-ray analysis indicated that the hydroxyl group of the formed hydroxyimino group adopts a cis configuration relative to the aromatic ring. This assignment is in agreement with previous observations[16,17,26] and is also as expected on a theoretical point of view[27] from an addition step on a triple bond. Another interesting feature is that in the amidine group, the CN bond distance between the central carbon and both nitrogen atoms are very similar (1.312/1.317 Å for **14c** and 1.335/1.325 for **15b**). This observation is in agreement with the delocalized character of the 'double bond'. These bonds are longer than in the localized CN double bond of the hydroxyimino group (1.291 and 1.289 Å for **14c** and **15b**, respectively).

The formation of compounds **14** and **15** may be explained by a similar mechanism as reported for acyclic nitroketene *S*,*S*-acetals **5** (Scheme 3).[17]

In this mechanism, compounds **12** and **13** undergo multiple protonation[16] and loss of a molecule of water, leading to the formation of transient conjugated hydroxynitrilium cations, **22** and **23**, which immediately react with the tethered phenyl ring by way of an electrophilic aromatic substitution mechanism, to afford the observed cationic compounds **24** and **25**.

The formation of cationic compounds **24** and **25** occurs through a rate-limiting step that requires heating at 60 °C. This may be explained by the fact that (poly)protonation of the starting molecule on both nitrogen atoms, slows down the water elimination step. In agreement with this assumption is the fact that with the less basic sulfur atom



Scheme 3. Suggested mechanism for the formation of **14** and **15**.

in series **4** or **5**, formation of the stable hydroxynitrilium ions occurs even at low temperature.[17,28]

At the end of the reaction, even when the acidity was quenched, compounds **14** and **15** were isolated as salts due to the strong basicity of the amidine group.[7]

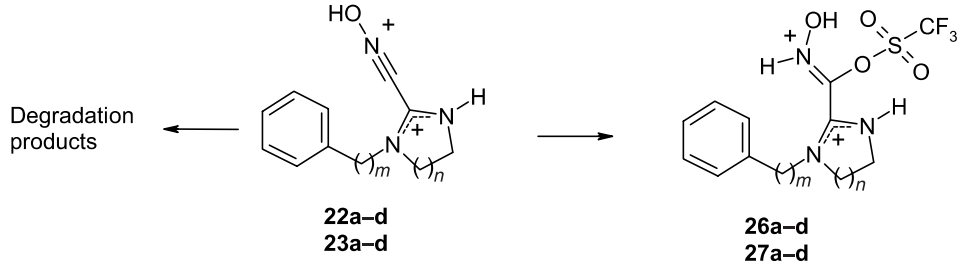
In the imidazoline series, the yields of isolated cyclization products **14a–c** varies, depending on the size of the formed ring; ranging from 62% for a seven-membered ring (**14a**) to 89% for the nine-membered ring (**14c**). As expected for reason of entropy, the yield in intramolecular cyclization drops to 13% for the 10-membered ring product **14d**.[29] The hexahydropyrimidine series **15a–c** follows the same pattern, with the yield decreasing regularly from 90% (seven-membered ring **15a**) to 72% (nine-membered ring **15c**) and dropping to 12% in the 10-membered ring product **15d**. In this case, the formed hydroxynitrilium ion can also either react (i) to afford degradation products or (ii) with triflate anion to form the nucleophilic addition compound, as previously observed in situ, with 1-amino-2-nitroethylene derivatives, affording ions **26** or **27** that easily decomposed during the hydrolysis step of the reaction medium (Scheme 4).[28]

The influence of the imidazoline ring or hexahydropyrimidine ring on the yield of this cyclization reaction is not very clear-cut.

NMR spectroscopy shows a sole (*E*)-isomer for the seven to nine-membered ring products **14a–c** and **15a–c**, but two sets of signals are observed for the 10-membered ring products **14d** and **15d**. These two sets of signals can be due to either (i) (*E*) and (*Z*) isomers or (ii) to a mixture of two conformers, formation of which would occur due to hampering of the flexing of the 10-membered ring by the presence of both the phenyl ring and the imidazoline, or hexahydropyrimidine, ring.[30]

3. Conclusion

The present study constitutes an extension of the use of acyclic 1-arylalkyl-substituted-2-nitroethylene diaminoacetals in the field of heterocyclic synthesis. Tricyclic hydroxyiminohydroazaazoniabenzocycloalkene trifluoromethanesulfonate derivatives can be easily prepared from 2-nitromethylene-1-(phenylalkyl)imidazolidine or 2-nitromethylene-1-(phenylalkyl)hexahydropyrimidine derivatives in trifluoromethanesulfonic acid. These derivatives



Scheme 4. Other suggested reactions for the formed hydroxynitrilium ions.

may be used in the field of natural products synthesis and work is in progress in this field.

4. Experimental

4.1. General remarks

Melting points were determined with a Büchi Melting point B545 apparatus using capillary tubes (temperature rate 2 °C/min) and were not corrected. A Brucker DPX 300 spectrometer, equipped with a low temperature probe, was used for ^{1}H, ^{9}F and ^{13}C NMR spectra recorded at 300.13, 282.37 and 75.47 MHz, respectively. NMR spectra were recorded at room temperature and chemical shifts reported relative to Me_4Si or $CFCl_3$ for fluorine. The reproducibility of ^{13}C NMR shift was about ± 0.05 ppm, depending on cell and concentration. Chemical assignments were made using DEPT135 technic and usual chemical shift assignments rules. Electron-impact ionization (70 eV) mass spectra were obtained with a Finnigan Incos 500 Instrument. High Resolution Mass Spectrometry was performed by the 'Centre Régional de Mesures Physiques de l'Ouest—Université de Rennes, France'. Flash chromatography was achieved on silica gel (20–45 μm particle size). HPLC was used to check the purity or to identify the various compounds described below. A Waters 600 pump equipped with a Rheodyne 7125 injector valve (20 μL loop) and an Applied Biosystem 785A programmable or Waters 486 UV detector at 254 nm, column 250×4 mm I.D., 5 μm Spherisorb silica or equivalent, were used with eluent CH_3CN:H_2O (with 1.5% AcOH) 70:30 and a 1 mL min^{-1} flow rate.

Trifluoromethanesulfonic acid was purchased from across and 1,1-bis(methylthio)-2-nitroethene from Lancaster and were used without further purification. No attempt was made to optimize the yields.

4.2. Starting material

4.2.1. 2-Nitromethylene-1-phenethylimidazolidine (12a). Typical procedure. *N′*-1′-Phenethylethane-1,2-diamine (1.75 g, 10.7 mmol) and 1,1-bis(methylthio)-2-nitroethene (1.76 g, 10.7 mmol) were heated at 60 °C in acetonitrile (30 mL) for 14 h under N_2. The advancement of the reaction was checked by thin-layer chromatography on silica gel deposited on aluminum sheet. The solution was concentrated under vacuum and the resulting residue was separated by flash chromatography with CH_2Cl_2–EtOH (97/3) and then crystallized from CH_2Cl_2/petroleum ether to afford compound **12a** as white crystals (1.92 g, 78%). Mp 99–98 °C (CH_2Cl_2/petroleum ether). ^{1}H NMR ($CDCl_3$): $\delta=2.87$ (t, $J=7.3$ Hz, 2H, –CH_2-Ph), 3.39 (t, $J=7.3$ Hz, 2H, –CH_2–N<), 3.46 (dd, $J=10.4$, 1.2 Hz, 1H, imidazolidine –CH_2–N<), 3.48 (br d, $J=9.5$ Hz, 1H, imidazolidine –CH_2–N<), 3.67 (d, $J=9.7$ Hz, 1H, imidazolidine –HN–CH_2–), 3.70 (br d, $J=11.1$ Hz, 1H, imidazolidine –HN–CH_2–), 6.54 (s, 1H, vinylic H), 7.10–7.25 (m, 3H, aromatic *o*-H and *p*-H), 7.30–7.39 (m, 2H, aromatic *m*-H), 8.60 (br s, 1H, N–H). ^{13}C NMR ($CDCl_3$): $\delta=33.7$ (*C*H_2-Ph), 42.4 (–*C*H_2–N<), 47.2 and 49.1 (imidazolidine CH_2), 96.4 (=*C*H–NO_2), 127.0, 128.6 and 128.8 (aromatic CH), 137.6 (*ipso*-C), 159.1 [>*C*=CH(NO_2)]. HRMS for $C_{12}H_{15}N_3O_2$ ([M^+]): calcd 233.1164, found 233.1155. HRMS for $C_{12}H_{15}N_2O$ ([M^+-NO]): calcd 203.1184, found 203.1181.

4.2.2. 2-Nitromethylene-1-(3-phenylpropyl)imidazolidine (12b). From *N′*-1′-(3-phenylpropyl)ethane-1,2-diamine (1.44 g, 8 mmol) and 1,1-bis(methylthio)-2-nitroethene (1.76 g, 8 mmol) in refluxed acetonitrile (25 mL) for 12 h. The desired compound **12b** crystallized as white crystals (1.25 g, 62%). Mp 117–118 °C (CH_2Cl_2/petroleum ether). ^{1}H NMR ($CDCl_3$): $\delta=1.90$ (q, $J=7.5$ Hz, 2H, –CH_2–CH_2–CH_2–), 2.63 (t, $J=7.5$ Hz, 2H, –CH_2-Ph), 3.12 (t, $J=7.4$ Hz, 2H, –CH_2–N<), 3.59 (m, 2H, imidazolidine –CH_2–N<), 3.70 (m, 2H, imidazolidine –HN–CH_2–), 6.48 (s, 1H, vinylic H), 7.16 (cd, $J=7.2$ Hz, 2H, aromatic *o*-H), 7.20 (ct, $J=7.3$ Hz, 1H, aromatic *p*-H), 7.29 (ct, $J=6.7$ Hz, 2H, aromatic *m*-H), 8.59 (br s, 1H, N–H). ^{13}C NMR ($CDCl_3$): $\delta=28.3$ (CH_2), 32.6 (*C*H_2-Ph), 42.1 (–*C*H_2–N<), 45.0 and 48.3 (imidazolidine CH_2), 96.4 (=*C*H–NO_2), 126.1, 128.0 and 128.4 (aromatic CH), 140.1 (*ipso*-C), 159.0 [>*C*=CH(NO_2)]. HRMS for $C_{13}H_{17}N_3O_2$ ([$M^{\cdot+}$]): calcd 247.13208, found 247.1334. HRMS for $C_{13}H_{17}N_2O$ ([$M-NO]^+$): calcd 217.1341, found 217.1335.

4.2.3. 2-Nitromethylene-1-(4-phenylbutyl)imidazolidine (12c). From *N′*-1′-(4-phenylbutyl)ethane-1,2-diamine (2.41 g, 12.5 mmol) and 1,1-bis(methylthio)-2-nitroethene (2.12 g, 12.8 mmol) in refluxed acetonitrile (25 mL) for 72 h. The resulting products were separated by flash chromatography: unreacted 1,1-bis(methylthio)-2-nitroethene (0.53 g, 25%) was first separated using CH_2Cl_2 as eluent, then compound **12c** (1.10 g, 33%) as white crystals. Mp 96–97 °C (CH_2Cl_2/petroleum ether). ^{1}H NMR ($CDCl_3$): $\delta=1.60$ (m, 4H, –CH_2–CH_2–), 2.63 (t, $J=6.9$ Hz, –CH_2-Ph), 3.10 (t, $J=6.9$ Hz, –CH_2–N<), 3.58 (complex t, $J_{app}=9.0$ Hz, 2H, imidazolidine –CH_2–N<), 3.71 (ct, $J_{app}=9.0$ Hz, 2H, imidazolidine –HN–CH_2–), 6.52 (s, 1H, vinylic H), 7.12–7.22 (m, 3H, aromatic *o*-H and *p*-H), 7.30 (m, 2H, aromatic *m*-H), 8.60 (br s, H, N–H). ^{13}C NMR ($CDCl_3$): $\delta=26.6$ (CH_2), 28.4 (CH_2), 35.4 (*C*H_2-Ph), 42.3 (–*C*H_2–N<), 45.6 and 48.5 (imidazolidine CH_2), 96.6 (=*C*H–NO_2), 126.1, 128.3 and 128.5 (aromatic CH), 141.4 (*ipso*-C), 159.3 [>*C*=CH(NO_2)]. HRMS for $C_{14}H_{19}N_3O_2$ ([M^+]): calcd 261.1477, found 261.1482. HRMS for $C_{14}H_{19}N_2O$ ([M^+-NO]): calcd 231.1497, found 231.1507. HRMS for $C_{14}H_{19}N_2$ ([M^+-NO_2]): calcd 215.1548, found 215.1545.

4.2.4. 2-Nitromethylene-1-(5-phenylpentyl)imidazolidine (12d). From *N′*-1′-(4-phenylpentyl)ethane-1,2-diamine (2.21 g, 10.7 mmol) and 1,1-bis(methylthio)-2-nitroethene (1.69 g, 10.2 mmol) at 50 °C in acetonitrile (30 mL) for 23 h was obtained on cooling compound **12d** (1.58 g, 56%) as light white crystals. Mp 115.8 °C (CH_2Cl_2/petroleum ether). ^{1}H NMR ($CDCl_3$): $\delta=1.33$ (m, 2H, –CH_2–CH_2–CH_2–), 1.59–1.67 (m, 4H, –CH_2–CH_2–CH_2–CH_2–), 2.62 (ct, $J=7.64$, 7.49 Hz, 2H, –CH_2-Ph), 3.09 (ct, $J=7.49$, 7.33 Hz, 2H, –CH_2–N<), 3.61 (m, 2H, imidazolidine –CH_2–N<), 3.73 (m, 2H, imidazolidine –HN–CH_2–), 6.52 (s, 1H, vinylic H), 7.15–7.21 (m, 3H, aromatic *o*-H and *p*-H), 7.26–7.31 (m, 2H, aromatic *m*-H), 8.62 (br s, H, N–H). ^{13}C NMR ($CDCl_3$): $\delta=26.6$ (CH_2), 27.1 (CH_2), 30.9 (CH_2),

35.6 (CH_2-Ph), 42.3 (–CH_2–N<), 45.6 and 48.6 (imidazolidine CH_2), 96.6 (=CH–NO_2), 125.9 and 128.4 (aromatic CH), 141.9 (*ipso*-C), 159.3 [>C=CH(NO_2)]. $C_{15}H_{21}N_3O_2$ (275.35): calcd C 65.49, H 7.63, N 15.34, found C 65.43, H 7.69, N 15.26.

4.2.5. 2-Nitromethylene-1-phenethylhexahydropyrimidine (13a). Typical procedure. *N*′-1′-Phenethylpropane-1,3-diamine (1.27 g, 7.1 mmol) and 1,1-bis(methylthio)-2-nitroethene (1.19 g, 7.2 mmol) were heated at 40 °C in acetonitrile (30 mL) for 18 h under N_2. The solution was concentrated under vacuum and the resulting product was purified by flash chromatography with CH_2Cl_2–EtOH (97/3) and then crystallized from CH_2Cl_2/petroleum ether to afford **13a** as light yellow crystals (1.33 g, 76%). Mp 113–114 °C (CH_2Cl_2/petroleum ether). ^{1}H NMR ($CDCl_3$): δ=1.86 (q, J=8.8 Hz, 2H, hexahydropyrimidine –CH_2–), 2.89 (t, J=7.2 Hz, 2H, –CH_2-Ph), 3.13 (t, J=5.8 Hz, 2H, –CH_2–N<), 3.34 (dd, J=5.6, 3.1 Hz, 2H, hexahydropyrimidine –CH_2–N<), 3.43 (t, J=7.2 Hz, 2H, hexahydropyrimidine –HN–CH_2–), 6.70 (s, 1H, vinylic H), 7.16–7.23 (m, 2H, aromatic *o*-H and *p*-H), 7.25–7.36 (m, 3H, 2 aromatic *m*-H and aromatic *o*-H), 10.72 (br s, 1H, N–*H*). ^{13}C NMR ($CDCl_3$): δ=19.7 (CH_2), 33.7 (CH_2-Ph), 37.5 (–CH_2–N<), 47.4 and 52.5 (hexahydropyrimidine CH_2), 97.8 [=CH(NO_2)], 126.7, 128.4 and 128.5 (aromatic CH), 137.0 (*ipso*-C), 153.8 [>C=CH(NO_2)]. HRMS for $C_{13}H_{17}N_3O_2$ ([M^+]): calcd 247.1321, found 247.1309. HRMS for $C_{13}H_{17}N_2O$ ([M^+−NO]): calcd 217.1341, found 217.1356.

4.2.6. 2-Nitromethylene-1-(3-phenylpropyl)hexahydropyrimidine (13b). From *N*′-1′-(3-phenylpropyl)propane-1,3-diamine (2.23 g, 11.6 mmol) and 1,1-bis(methylthio)-2-nitroethene (1.99 g, 12 mmol) at 40 °C in acetonitrile (30 mL) for 18 h. Compound **13b** (1.95 g, 64%) was obtained as light yellow crystals. Mp 126–127 °C (CH_2Cl_2/petroleum ether). ^{1}H NMR ($CDCl_3$): δ=1.87 (m, 2H, hexahydropyrimidine –CH_2–), 2.00 (m, 2H, CH_2–CH_2–CH_2), 2.62 (t, J=7.6 Hz, 2H, –CH_2-Ph), 3.16 (d, J=8.0 Hz, 1H, –CH_2–N<), 3.19 (d, J=7.8 Hz, 1H, –CH_2–N<), 3.30–3.40 (m, 4H, hexahydropyrimidine –HN–CH_2– and –CH_2–N<), 6.61 (s, 1H, vinylic H), 7.12–7.24 (m, 3H, aromatic *o*-H and *p*-H), 7.26–7.32 (m, 2H, aromatic *m*-H), 10.70 (br s, 1H, N–H). ^{13}C NMR ($CDCl_3$): δ=20.6 (CH_2), 29.2 (CH_2), 33.1 (CH_2-Ph), 38.2 (–CH_2–N<), 47.3 and 51.2 (hexahydropyrimidine CH_2), 98.5 [=CH(NO_2)], 126.7, 128.5 and 129.0 (aromatic CH), 140.6 (*ipso*-C), 154.5 [>C=CH(NO_2)]. HRMS for $C_{14}H_{19}N_3O_2$ ([M^+]): calcd 261.1477, found 261.1480. HRMS for $C_{14}H_{19}N_2O$ ([M^+−NO]): calcd 231.1497, found 231.1496. HRMS for $C_{14}H_{19}N_2$ ([M^+−NO_2]): calcd 215.1548, found 215.1537.

4.2.7. 2-Nitromethylene-1-(4-phenylbutyl)hexahydropyrimidine (13c). From *N*′-1′-(4-phenylbutyl)propane-1,3-diamine (3.63 g, 17.8 mmol) and 1,1-bis(methylthio)-2-nitroethene (2.81 g, 17.0 mmol) at 52 °C in acetonitrile (30 mL) for 15 h. Compound **13c** (2.40 g, 69%) was obtained as light yellow crystals. Mp 127–128 °C (CH_2Cl_2/petroleum ether). ^{1}H NMR ($CDCl_3$): δ=1.61 (m, 4H, –CH_2–CH_2–), 1.98 (q, J=5.9 Hz, 2H, hexahydropyrimidine –CH_2–), 2.63 (ct, J=6.9 Hz, 2H, –CH_2-Ph), 3.15 (ct, J=7.3 Hz, 2H, –CH_2–N<), 3.33 (t, J=5.8 Hz, 2H, hexahydropyrimidine –CH_2–N<), 3.38 (m, 2H, hexahydropyrimidine –HN–CH_2–), 6.62 (s, 1H, vinylic H), 7.13–7.23 (m, 3H, aromatic *o*-H and *p*-H), 7.25–7.34 (m, 2H, aromatic *m*-H), 10.70 (br s, 1H, N–*H*). ^{13}C NMR ($CDCl_3$): δ=20.0 (CH_2), 26.8 (CH_2), 28.2 (CH_2), 35.2 (CH_2-Ph), 37.6 (–CH_2–N<), 46.7 and 50.9 (hexahydropyrimidine CH_2), 97.9 (=CH–NO_2), 125.8, 128.1 and 128.2 (aromatic CH), 141.2 (*ipso*-C), 153.8 [>C=CH(NO_2)]. HRMS for $C_{15}H_{21}N_3O_2$ ([M^+]): calcd 275.1634, found 275.1636. HRMS for $C_{14}H_{19}N_2O$ ([M^+−NO]): calcd 245.1654, found 245.1652.

4.2.8. 2-Nitromethylene-1-(5-phenypentyl)hexahydropyrimidine (13d). From *N*′-1′-(5-phenylpentyl)propane-1,3-diamine (1.0 g, 4.5 mmol) and 1,1-bis(methylthio)-2-nitroethene (0.75 g, 4.5 mmol) at 55 °C in acetonitrile (15 mL) for 17 h. Compound **13d** (0.99 g, 82%) was obtained as yellow crystals. Mp 112.8 °C (CH_2Cl_2/petroleum ether). ^{1}H NMR ($CDCl_3$): δ=1.30 (m, 2H, –CH_2–), 1.62 (m, 4H, –CH_2–CH_2–CH_2–CH_2–), 2.01 (q, J=5.95 Hz, 2H, hexahydropyrimidine –CH_2–), 2.62 (t, J=7.57 Hz, 2H, –CH_2-Ph), 3.13 (dd, J=7.87, 7.77 Hz, 2H, –CH_2–N<), 3.33 (ct, J_{app}=5.75 Hz, 2H, hexahydropyrimidine –CH_2–N<), 3.40 (m, 2H, hexahydropyrimidine –HN–CH_2–), 6.62 (s, 1H, vinylic-H), 7.15–7.22 (m, 3H, aromatic *o*-H and *p*-H), 7.29–7.61 (m, 2H, aromatic *m*-H), 10.75 (br s, 1H, N–H). ^{13}C NMR ($CDCl_3$): δ=20.6 (CH_2), 26.5 (CH_2), 27.8 (CH_2), 31.4 (CH_2), 36.1 (CH_2-Ph), 38.2 (–CH_2–N<), 47.4 and 51.7 (hexahydropyrimidine CH_2), 98.6 (=CH–NO_2), 126.2 and 128.7 (aromatic CH), 142.3 (*ipso*-C), 154.4 [>C=CH(NO_2)]. HRMS for $C_{16}H_{23}N_3O_2$ ([M^+]): calcd 289.1790, found 289.1797. HRMS for $C_{16}H_{23}N_2O$ ([M^+−NO]): calcd 259.1810, found 259.1802. HRMS for $C_{16}H_{23}N_2$ ([M^+−NO_2]): calcd 243.1861, found 243.1863.

4.3. Cyclic compounds. Typical procedure

4.3.1. 4-[(*E*)-Hydroxyimino]-2,4,9,10-tetrahydro-1*H*-10a-aza-3-azoniabenzo[*f*]azulene trifluoromethanesulfonate (14a). 2-Nitroethylene-1-(4-phenethyl)imidazolidine (233 mg, 1.0 mmol) was dissolved in trifluoromethanesulfonic acid (4.4 mL, 50 mmol). The solution was heated to 60 °C for 24 h. After cooling, the solution was poured over ice (15 g) and anhydrous Na_2CO_3 (6.0 g, 56.6 mmol). The aqueous phase was quickly extracted with CH_2Cl_2–MeOH (95/5) (4×50 mL). The organic phases were dried over $MgSO_4$ and the solvent evaporated under reduced pressure. The resulting product was purified by flash chromatography with CH_2Cl_2–MeOH (95/5) and then crystallized from CH_2Cl_2/petroleum ether to afford **14a** (227 mg, 62%) as white crystals. Mp 191–192 °C (CH_2Cl_2/petroleum). ^{1}H NMR ($CDCl_3$-[d_6]DMSO): δ=3.13 (s, 2H, –CH_2-Ph), 3.59 (br s, 2H, –CH_2–N<), 3.83 (t, J=10.8 Hz, 2H, imidazolidine –CH_2–N<), 4.05 (t, J=10.5 Hz, 2H, imidazolidine –CH_2–N=), 7.41 (m, 3H, aromatic H), 7.52 (d, J=7.5 Hz, 1H, aromatic H), 9.87 (br s, 1H, =NH–), 13.03 (br s, 1H, >=N–OH). ^{13}C NMR ($CDCl_3$-[d_6]DMSO): δ=31.6 (CH_2-Ph), 42.4 (CH_2), 49.7 (CH_2), 54.3 (CH_2), 121.5 (q, J^1_{CF}=321 Hz, $CF_3SO_3^-$), 127.6 and 128.6 (aromatic CH), 129.9 and 130.9 (aromatic CH), 132.0 (*ipso*-C), 137.6 (*ipso*-C), 142.2 (>C=N–H), 160.1 (>C=N–OH). ^{19}F NMR (282.37 MHz, $CDCl_3$-[d_6]DMSO): δ=−78.40 ($CF_3SO_3^-$).

HRMS for $C_{12}H_{13}N_3O$ ([$M^+ - CF_3SO_3H$]): calcd 215.1057, found 215.1070.

4.3.2. 11-[(*E*)-Hydroxyimino]-2,3,4,5,6,11-hexahydro-3a-aza-1-azoniabenzo[*a*]cyclopenta[*d*]cyclooctene trifluoromethanesulfonate (14b). From 2-nitroethylene-1-(4-phenylpropyl)imidazolidine (247 mg, 1.0 mmol) was obtained cyclic compound as the triflate salt **14b** (299 mg, 79%), white crystals. Mp 160.7 °C (CH_2Cl_2/petroleum). ^{1}H NMR ([d_6]acetone): δ=1.86 (m, 2H, –CH_2–CH_2–CH_2–), 2.68 (t, J=6.5 Hz, 2H, –CH_2-Ph), 3.18 (m, 2H, CH_2–N<), 3.88 (t, J=10.3 Hz, 2H, imidazolidine –CH_2–N<), 4.26 (t, J=11.0 Hz, imidazolidine –CH_2–N=), 7.26 (t, J=7.5 Hz, 2H, aromatic H), 7.40 (t, J=8.0 Hz, 2H, aromatic H), 9.11 (br s, 1H, =N–H), 12.40 (vbs, 1H, >=N–OH). ^{13}C NMR ([d_6]acetone): δ=29.9 (CH_2), 30.1 (*C*H_2-Ph), 43.5 (CH_2), 45.2 (CH_2), 55.4 (CH_2), 122.9 (q, J_{CF}=321 Hz, $CF_3SO_3^-$), 128.5 and 128.8 (aromatic CH), 130.9 and 132.9 (aromatic CH), 133.3 (*ipso*-C), 139.5 (*ipso*-C), 144.8 (>C=N–H), 162.9 (>C=N–OH). ^{19}F NMR (282.37 MHz, [d_6]acetone): δ=−77.29 ($CF_3SO_3^-$). MS (70 eV); *m*/*z* (%): 229 (50) [$M^+ - CF_3SO_3H$], 228 (70) [$M^+ - CF_3SO_3H$–H], 212 (25) [$M^+ - CF_3SO_3H$–OH], 184 (20), 69 (100). HRMS for $C_{13}H_{15}N_3O$ ([$M^+ - CF_3SO_3H$]): calcd 229.1215, found 229.1205.

4.3.3. 12-[(*E*)-Hydroxyimino]-2,4,5,6,7,12-hexahydro-3*H*-3a-aza-1-azoniabenzo[*a*]cyclopenta[*d*]cyclononene trifluoromethanesulfonate (14c). From 2-nitroethylene-1-(4-phenylbutyl)imidazolidine (261 mg, 1.0 mmol) was obtained compound **14c** (351 mg, 89%) as white crystals. Mp 197.5 °C (CH_2Cl_2/petroleum). ^{1}H NMR ([d_6]acetone): δ=1.82 (m, 4H, –CH_2–CH_2–), 2.81 (br t, J=6.3 Hz, 2H, –CH_2-Ph), 3.40 (br t, J=5.5 Hz, 2H, CH_2–N<), 4.12 (ddd, J=12.5, 2.50, 1.56 Hz, 2H, imidazolidine –CH_2–N=), 4.30 (ddd, J=12.5, 2.50, 1.56 Hz, 2H, imidazolidine –CH_2–N<), 7.26–7.32 (m, 1H, aromatic H), 7.36–7.42 (m, 2H, aromatic H), 7.44–7.48 (m, 1H, aromatic H), 10.92 (br s, 2H, =N–H and >=N–OH). ^{13}C NMR ([d_6]acetone): δ=25.4 (CH_2), 27.6 (CH_2), 33.6 (*C*H_2-Ph), 44.7 (CH_2), 45.8 (CH_2), 53.4 (CH_2), 123.0 (q, J_{CF}=321 Hz, *C*$F_3SO_3^-$), 128.4 and 130.38 (aromatic CH), 130.41 and 132.1 (aromatic CH), 132.5 (*ipso*-C), 143.1 (*ipso*-C), 146.7 (>C=N–H), 163.7 (>C=N–OH). ^{19}F NMR (282.37 MHz, [d_6]acetone): δ=−79.28 ($CF_3SO_3^-$). MS (70 eV); *m*/*z* (%): 243 (42) [$M^+ - CF_3SO_3H$], 225 (98) [$M^+ - CF_3SO_3H$–OH], 197 (45), 116 (75) [$C_7H_6CN^+$], 56 (100). HRMS for $C_{14}H_{15}N_3$ ([$M^+ - CF_3SO_3H$–OH]): calcd 225.1266, found 225.1256.

4.3.4. 2-Hydroxyimino-7-aza-4-azoniatricyclo-[11.4.0.0.^{3,7}]heptadeca-1(17),3,13,15-tetraene trifluoromethanesulfonate (14d) From 2-nitromethylene-1-(5-phenylpentyl)imidazolidine (276 mg, 1 mmol) was obtained compound **14d** (54 mg, 13%) as white crystals. Mp 149.1 °C (CH_2Cl_2/petroleum). ^{1}H NMR ([D_6]acetone): δ=1.16 (massif, 2H, –CH_2–CH_2–CH_2–), 1.64 (m, 2H, –CH_2–CH_2–N<), 1.73 (m, 2H, Ph-CH_2–CH_2–), 2.56 (dd, J=5.8 Hz, 2H, –CH_2-Ph), 3.40 (dd, J=5.9 Hz, 2H, CH_2–N<), 4.03 (m, 2H, imidazolidine –CH_2–N<), 4.10 (m, 2H, imidazolidine, –CH_2–N=), 7.23–7.32 (m, 2H, aromatic H), 7.34–7.40 (m, 1H, aromatic H), 7.53 (m, 1H, aromatic H). ^{13}C NMR ([d_6]acetone): δ=22.7*, 21.8 (CH_2), 27.9, 25.8* (CH_2), 30.6*, 30.4 (CH_2), 31.2*, 32.6 (*C*H_2-Ph), 34.7*, 34.2 (CH_2), 43.9, 43.4* (CH_2), 46.7*, 46.7 (CH_2), 51.8*, 50.7 (CH_2), 127.7 and 127.9* (aromatic CH), 131.0* and 131.5 (aromatic CH), 131.8, 131.7* (*ipso*-C), 144.2*, 142.6 (*ipso*-C), 145.0, 144.6* (>C=N–H), 162.5, 163.8* (>C=N–OH) {* signals from the second isomer}. ^{19}F NMR (282.37 MHz, [d_6]acetone): δ=−78.47 ($CF_3SO_3^-$). HRMS for $C_{15}H_{18}N_3$ ([$M^+ - CF_3SO_3H$–OH]): calcd 240.1501, found 240.1494.

4.3.5. 5-[(*E*)-Hydroxyimino]-1,2,3,5,10,11-hexahydro-11a-aza-4-azoniadibenzo[*a*,*d*]cycloheptene trifluoromethanesulfonate (15a). From 2-nitroethylene-1-(4-phenethyl) hexahydropyrimidine (247 mg, 1.0 mmol) was obtained compound **15a** (342 mg, 90%) as white crystals. Mp 193–195 °C (CH_2Cl_2/petroleum). ^{1}H NMR ([d_6]-acetone): δ=2.23 (q, J=5.8 Hz, 2H, hexahydropyrimidine –CH_2–), 3.33 (t, J=5.6 Hz, 2H, CH_2-Ph), 3.62 (t, J=5.5 Hz, –CH_2–N<), 3.88 (t, J=5.7 Hz, 2H, hexahydropyrimidine CH_2–N<), 4.03 (t, J=5.6 Hz, 2H, hexahydropyrimidine CH_2–N=), 7.34 (dt, J=7.4, 1.5 Hz, 1H, aromatic H), 7.37 (dd, J=7.0, 1.4 Hz, 1H, aromatic H), 7.45 (dt, J=7.4, 1.4 Hz, 1H, aromatic H), 7.71 (dd, J=7.8, 1.4 Hz, 1H, aromatic H), 9.42 (br s, 1H, =N–H), 12.14 (br s, 1H, =N–OH). ^{13}C NMR ([d_6]acetone): δ=20.6 (CH_2), 32.6 (*C*H_2-Ph), 40.3 (CH_2), 48.8 (CH_2), 53.0 (CH_2), 122.8 (q, J^1_{CF}=321 Hz, C*F*$_3SO_3^-$), 127.7 and 127.7 (aromatic CH), 131.9 and 132.3 (aromatic CH), 132.5 (*ipso*-C), 138.3 (*ipso*-C), 148.0 (>C=N–H), 159.7 (>C=N–OH). ^{19}F NMR (282.37 MHz, [d_6]acetone): δ=−79.56 ($CF_3SO_3^-$). MS (70 eV); *m*/*z* (%): 229 (35) [$M^+ - CF_3SO_3H$], 228 (70) [$M^+ - CF_3SO_3H$–H], 213 (55), 212 (100) [$M^+ - CF_3SO_3$-H–OH], 184 (80). HRMS for $C_{13}H_{15}N_3O$ ([$M^+ - CF_3SO_3H$]): calcd 229.1215, found 229.1210.

4.3.6. 12-[(*E*)-Hydroxyimino]-3,4,5,6,7,12-hexahydro-2*H*-4a-aza-1-azoniadibenzo[*a*,*d*]cyclooctene trifluoromethanesulfonate (15b). From 2-nitroethylene-1-(4-phenylpropyl)hexahydropyrimidine (261 mg, 1.0 mmol) was obtained compound **15b** (334 mg, 85%) as white crystals. Mp 154–155 °C (acetone/petroleum ether). ^{1}H NMR ([d_6]acetone): δ=2.04 (m, 2H, hexahydropyrimidine –CH_2–), 2.19 (q, J=5.8 Hz, 2H, –CH_2–CH_2–CH_2–), 2.87 (t, J=6.1 Hz, –CH_2-Ph), 3.64 (t, J=5.6 Hz, –CH_2–N<), 3.69 (t, J=5.3 Hz, 2H, hexahydropyrimidine –CH_2–N<), 3.84 (t, J=5.6 Hz, 2H, hexahydropyrimidine –CH_2–N=), 7.34 (d, J=7.6 Hz, 1H, aromatic H), 7.35 (dt, J=7.6, 1.5 Hz, 1H, aromatic H), 7.45 (dt, J=7.4, 1.5 Hz, 1H, aromatic H), 7.59 (d, J=7.9 Hz, 1H, aromatic H), 9.54 (br s, 1H, =N–H), 12.10 (br s, 1H, =N–OH). ^{13}C NMR ([d_6]acetone): δ=20.7 (CH_2), 29.8 (CH_2), 33.5 (*C*H_2-Ph) (br and weak signal), 40.7 (CH_2), 50.9 (CH_2), 54.2 (CH_2) (br and weak signal), 123.0 (q, J_{CF}=321 Hz, *C*$F_3SO_3^-$), 127.4 and 130.5 (aromatic CH), 130.6 and 130.8 (aromatic CH), 131.7 (*ipso*-C), 139.6 (*ipso*-C), 147.9 (>C=N–H), 158.2 (>C=N–OH). ^{19}F NMR (282.37 MHz, [d_6]acetone): δ=−81.27 ($CF_3SO_3^-$). MS (70 eV); *m*/*z* (%): 243 (45) [$M^+ - CF_3SO_3H$], 242 (87) [$M^+ - CF_3SO_3H$–H], 226 (30) [$M^+ - CF_3SO_3$-H–OH], 98 (100). HRMS for $C_{14}H_{17}N_3O$ ([$M^+ - CF_3SO_3H$]): calcd 243.1372, found 243.1368. Analysis: $C_{15}H_{18}F_3N_3SO_4$ (393.38): calcd C 46.89, H 4.78, N 10.49, S 8.19; found C 45.80, H 4.58, N 10.7, S 8.14.

4.3.7. 13-[(*E*)-Hydroxyimino]-2,3,4,5,6,7,8,13-octahydro-4a-aza-1-azoniadibenzo[*a*,*d*]cyclononene trifluoromethanesulfonate (15c). From 2-nitroethylene-1-(4-phenylpropyl)hexahydropyrimidine (275 mg, 1.0 mmol) was obtained compound **15c** (294 mg, 72%) as white crystals. Mp 182.9 °C (CH_2Cl_2/petroleum). ^{1}H NMR ([d_6]acetone): δ=1.77 (br s, 4H, –C*H*$_2$–C*H*$_2$–), 2.28 (quintuplet, J=6.0 Hz, 2H, hexahydropyrimidine –CH_2–), 2.87 (m, 2H, –C*H*$_2$-Ph), 3.72 (br t, J=4.5 Hz, 2H, CH_2–N<), 3.87 (m, 4H, hexahydropyrimidine CH_2–N< and –CH_2–N=), 7.35–7.45 (m, 2H, aromatic H), 7.45–7.55 (m, 2H, aromatic H), 8.56 (br s, 1H, =N–H), 10.57 (br s, 1H, =N–OH). ^{13}C NMR ([d_6]acetone): δ=19.6 (CH_2), 26.4 (CH_2), 27.6 (CH_2), 29.1 (*C*H$_2$-Ph), 39.8 (CH_2), 48.4 (CH_2), 50.4 (CH_2), 122.1 (q, J_{CF}=321 Hz, *C*$F_3SO_3^-$), 127.5 and 129.1 (aromatic CH), 130.6 and 130.9 (aromatic CH), 131.4 (*ipso*-C), 141.9 (*ipso*-C), 148.4 (>C=N–H), 158.2 (>C=N–OH). ^{19}F NMR (282.37 MHz, [d_6]acetone): δ=−74.14 ($CF_3SO_3^-$). MS (70 eV); *m*/*z* (%): 257 (8) [M^+−CF_3SO_3H], 240 (75) [M^+−CF_3SO_3H–OH], 116 (80), 98 (100). HRMS for $C_{15}H_{19}N_3O$ ([M^+−CF_3SO_3H]): calcd 257.1528, found 257.1547. HRMS for $C_{15}H_{18}N_3$ ([M^+−CF_3SO_3H–OH]): calcd 240.1501, found 240.1494.

4.3.8. 2-Hydroxyimino-8-aza-4-azoniatricyclo-[12.4.0.0.^{3,8}]octadeca-1(18),3,14,16-tetraene trifluoromethanesulfonate (15d) From 2-nitroethylene-1-(5-phenylpentyl)hexahydropyrimidine (289 mg, 1 mmol) was obtained compound **15d** (50 mg, 12%) as white crystals. Mp 201.2 °C (CH_2Cl_2/petroleum). ^{1}H NMR ([d_6]methanol): δ=1.17 (m, 2H, –CH_2–C*H*$_2$–CH_2–), 1.80–1.84 (massif, 4H, –C*H*$_2$–CH_2–C*H*$_2$–), 2.08–2.10 (ct, J=5.77 Hz, 2H, hexahydropyrimidine, –CH_2–), 2.70–2.75 (dd, J=6.5 Hz, 2H, –C*H*$_2$-Ph), 3.51–3.61 (m, 4H, –CH_2–N< and hexahydropyrimidine –CH_2–N<), 3.90 (dd, J=5.8 Hz, 2H, hexahydropyrimidine –C*H*$_2$–N=), 7.30–7.35 (m, 2H, aromatic H), 7.37–7.44 (m, 1H, aromatic H), 7.95 (m, 1H, aromatic H). ^{13}C NMR ([d_6]methanol) mixture of isomers: δ=19.89*, 19.71 (CH_2), 24.86, 24.86* (CH_2), 28.19, 26.38* (CH_2), 33.47, 33.38* (CH_2), 37.67, 37.67* (*C*H$_2$-Ph), 40.46, 40.11* (CH_2), 48.18*, 46.82 (CH_2), 54.64*, 53.65 (CH_2), 125.98, 123.93* and 127.83*, 127.64 (aromatic CH), 131.20, 130.92* and 131.47, 131.34* (aromatic CH), 132.84*, 131.83 (*ipso*-C), 145.95, 142.66* (*ipso*-C), 149.39*, 148.35 (>C=N–H), 159.26, 159.01* (>C=N–OH) {* signals from the second isomer}. ^{19}F NMR (282.37 MHz, [d_6]acetone): δ=−77.00 ($CF_3SO_3^-$). HRMS for $C_{16}H_{20}N_3$ ([M^+−CF_3SO_3H–OH]): calcd 254.1657, found 254.1672.

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References and notes

1. Charette, A. B.; Grenor, M. *Tetrahedron Lett.* **2000**, *41*, 1677–1680.
2. Hida, T.; Tsubotani, S.; Funabashi, Y.; Ono, H.; Harada, S. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 863–869.
3. Buschi, C. A.; Pomilio, A. B. *Phytochemistry* **1987**, *26*, 863–865.
4. De la Rosa, R.; Martinez-Barraza, V.; Burgos, C.; Alvarez-Builla, J. *Tetrahedron Lett.* **2000**, *41*, 5837–5840.
5. Naka, M.; Nanbu, T.; Kobayashi, K.; Kamanaka, Y.; Komeno, M.; Yanasa, R.; Fukutomi, T.; Fujimura, S.; Seo, N. G.; Fujiwara, N.; Ohuchida, S.; Suzuki, K.; Kondo, K.; Taniguchi, N. *Biochem. Biophys. Res. Commun.* **2000**, *270*, 663–667.
6. Tucker, J. A.; Clyton, T. L.; Chidester, C. G.; Schulz, M. W.; Harrington, L. E.; Conrad, S. J.; Yagi, Y.; Oien, N. L.; Yurek, D.; Kuo, M.-S. *Bioorg. Med. Chem.* **2000**, *8*, 601–615.
7. Häfelinger, G.; Kuske, F. K. H. In *The Chemistry of Amidine and Imidate*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1991; pp 1–93; and references cited therein.
8. (a) Wendt, M. D.; Rockway, T. W.; Geyer, A.; McClellan, W.; Weitzberg, M.; Zhao, X.; Mantei, R.; Nienaber, V. L.; Stewart, K.; Klinghofer, V.; Giranda, V. L. *J. Med. Chem.* **2004**, *47*, 303–324. (b) Kahan, F. M.; Kropp, H.; Sundelof, J. G.; Birnbaum, J. *J. Antimicrob. Chemother.* **1983**, *12*, 1–35.
9. (a) Reddy, B. S. P.; Sondhi, S. M.; Lown, J. W. *Pharmacol. Ther.* **1999**, *84*, 1–111. (b) Szulawska, A.; Gniazdowski, M.; Czyz, M. *Biochem. Pharmacol.* **2005**, *69*, 7–17.
10. Bailey, C.; Baku, E.; Hayler, J.; Kane, P. *Tetrahedron Lett.* **1999**, *40*, 4847–4850.
11. Pinner, A. *Ber.* **1885**, *18*, 2845–2852.
12. Stilz, H. U.; Jablonka, B.; Just, M.; Knoll, J.; Paulus, E. F.; Zoller, G. *J. Med. Chem.* **1996**, *39*, 2118–2122.
13. Thurkauf, A. *J. Label. Compd. Radiopharm.* **1997**, *39*, 123–128.
14. Judkins, B. D.; Allen, D. G.; Cook, T. A.; Evans, B.; Sardharwala, T. A. *Synth. Commun.* **1996**, *26*, 4351–4367.
15. Lange, U. E. W.; Schäfer, B.; Baucke, D.; Buschmann, E.; Mack, H. *Tetrahedron Lett.* **1999**, *40*, 7067–7071.
16. Coustard, J.-M. *Tetrahedron* **1996**, *52*, 9509–9520.
17. Coustard, J.-M. *Eur. J. Org. Chem.* **2001**, 1525–1531.
18. Rajappa, S. *Tetrahedron* **1999**, *55*, 7065–7114.
19. Pavlova, Z. F.; Lipina, E. S.; Perekalin, V. V. *Sulfur Rep.* **1995**, *16*, 149–172.
20. Kearney, T.; Harris, P. A.; Jackson, A.; Joule, J. A. *Synthesis* **1992**, *8*, 769–772.
21. Reddy, K. V.; Rajappa, S. *Heterocycles* **1994**, *37*, 347–354.
22. Breitmaier, E.; Vœlter, W. *Carbon-13 NMR Spectroscopy: High-Resolution Methods and Applications in Organic Chemistry and Biochemistry*, 3rd ed. 1987 pp 272–293.
23. (a) The atomic coordinates for **14c** (deposition number CCDC 291924) and **15b** (deposition number CCDC 291923) are available upon request from the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK. The crystallographic numbering system differs from that used in the text; therefore, any request should be accompanied by the full literature citation of this paper. (b) The crystal representations in this paper were produced using the Mercury 1.4.1 software from the Cambridge Crystallographic Data Centre. http://www.ccdc.cam.ac.uk/mercury/.

24. Sheldrick, G. M. *SHELXS86: Programme for the Solution of Crystal Structures*; University of Göttingen: Göttingen, Germany, 1985.
25. Watkins, D. J.; Carruthers, J. R.; Betteridge, P. W. *Crystals Software; Chemical Crystallography Laboratory*; University of Oxford: England, 1985.
26. Coustard, J.-M. *Tetrahedron* **1995**, *51*, 10929–10940.
27. Hegarty, A. F. *Acc. Chem. Res.* **1980**, *13*, 448–454.
28. Coustard, J.-M. *Tetrahedron* **1999**, *55*, 5809–5820.
29. Eliel, E. L.; Wilen, S. H.; Mander, L. N. Stereochemistry of Organic Compounds; Wiley: New York-Chichester-Brisbane-Toronto-Singapore, 1994; pp 675–685.
30. Strenge, A.; Rademacher, P. *Eur. J. Org. Chem.* **1999**, *7*, 1601–1609 and references cited therein.