J. Chem. Sci., Vol. 119, No. 3, May 2007, pp. 259–265.

New amidines from intramolecular cyclization in triflic acid of nitroketene aminals with a tethered phenyl ring

SORO YAYA,[a,*] BAMBA FANTÉ,[b] SIAKA SORHO,[a] COUSTARD JEAN-MARIE[b] and ADIMA A AUGUSTIN[a]

[a]Laboratoire des Procédés Industriels de Synthèse et d'Environnement, Institut National Polytechnique Félix Houphouët-Boigny, BP 991 Yamoussoukro, Côte d'Ivoire
[b]Laboratoire 'Synthèse et Réactivité des Substances Naturelles', UMR 6514, 40, Avenue du Recteur Pineau, F-86022 Poitiers, France
e-mail: soro_y@yahoo.fr

MS received 12 September 2006; revised 22 May 2007

Abstract. Nitroketene aminals with a tethered phenyl group underwent an intramolecular cyclization in trifluoromethanesulfonic acid to afford the corresponding N-(3-ethyl-hydrohydroxyiminobenzocycloalkenylidene)methylamine trifluoromethanesulfonate. The yields were fair to good excepted for the starting compound 1-[N-ethyl-N-(2-phenylethyl)amino]-1-methylamino-2-nitroethene.

Keywords. Nitroketene S,N-acetals; nitroketene aminals; trifluoromethanesulfonic acid; cyclic triflate salt; cyclization; amidine.

1. Introduction

The amidine functionality has been found in many natural products and amidine containing molecules are found to play a crucial role in many biological processes.[1,2] The amidine moiety is an important pharmacophore in active ingredients of drugs.[3,4] They are versatile building blocks for the synthesis of various heterocyclic compounds.[5] In particular, aromatic amidines have been shown to function as excellent arginine side-chain mimetic due to their favorable spatial and electrostatic properties.[6]

Some N-Aryl substituted derivatives show insecticidal activity against the housefly, *muska domestica*, and special binding activity towards the nicotinic acetylcholine receptor.[7] They are also of interest as naturally occurring constituents of t-RNA[8] and show significant inhibition activity in oedema as well as anti-inflammatory and analgesic activities.[9]

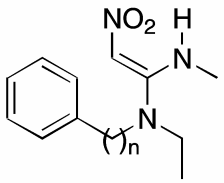
Consequently, a plethora of methods has been developed for preparation of amidines[10] from amides, nitriles or thioamides, and involve highly acidic,[11] alkaline[12] or strongly reducing reaction conditions.[13] Alternative mild methods involving the reduction of amidoximes[14] or the conversion of esters derivatives[15] have also been reported.

Recently, we reported the cyclization of 1-benzylamino-1-methylsulfanyl-2-nitroethenes in triflic acid leading to formation of the corresponding diazadihydroacenaphthylene derivatives with an isoxazoline ring.[16] In the present paper the synthesis of new amidines as triflate salts, starting from nitroketene aminals in trifluoromethanesulfonic acid (triflic acid) is described.

2. Results and discussion

2.1 *Starting material*

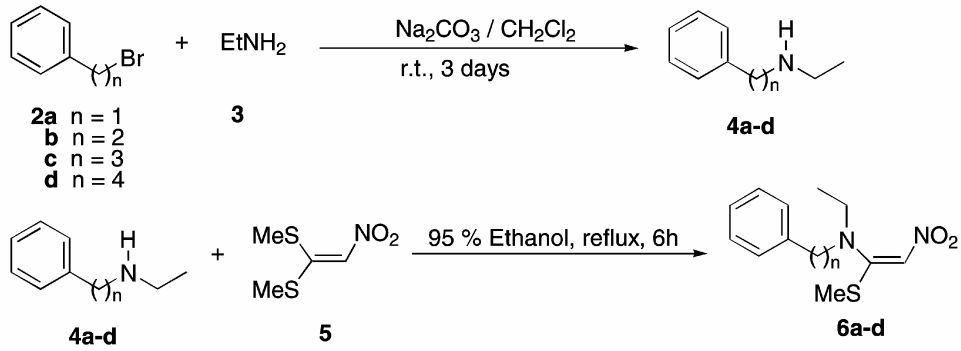
The starting materials **1a–d** (figure 1) are unsymmetrical nitroketene aminals belonging to the 1,1-



1a-d

Figure 1. Starting materials **1a–d**.

*For correspondence



Scheme 1. Synthesis of nitroketene *S,N*-acetals **6a–d**.

Table 1. Yields of the formed nitroketene *S,N*-acetals **6a–d**.

Starting diamine	**4a**	**4b**	**4c**	**4d**
Product	**6a**	**6b**	**6c**	**6d**
Yield (%)	52	56	40	36

bis(alkylamino)-2-nitromethylene derivatives with a tethered phenyl group on one of the nitrogen atom.

They are prepared from 1,1-*bis*(methylthio)-2-nitroethene in a conventional way by two successive nucleophilic substitutions:[17,18] the fist one, with about one molar equivalent of the corresponding N-ethyl-N-(*ω*-phenylalkyl)amine and, the second one, with two molar equivalents of aqueous solution of methylamine.

The N-ethyl-N-(*ω*-phenylalkyl)amines **4** were prepared on a conventional way from the reaction of the corresponding 1-bromo-*ω*-phenylalkyl derivative **2** with an excess of aqueous solution of ethylamine **3** (scheme 1).

In equimolar equivalent, the nucleophilic substitution between amine **4** and 1,1-*bis*(methylthio)-2-nitroethene **5** lead to the formation of the expected nitroketene aminals **6**. These reactions proceeded in yields varying from 56 to 36%, decreasing with the length of the alkyl chain, probably because of entropic reason (table 1). As expected, a small amount of the di-substituted compounds was also observed.

Compounds **6** were mainly characterized by NMR and HRMS spectroscopy. The NMR spectra show thiomethyl and vinylic protons both resonating as a singulet in the range δ_H 1·15–1·19 ppm and 6·83–6·89 ppm respectively. The nitromethylene carbons =<u>C</u>H–NO_2 are observed at δ_C 111·7–112·9 ppm and the ><u>C</u>=C ethylene carbons in the range δ_C 166·9–167·5 ppm. The thiomethyl carbons are closed to 13 ppm.

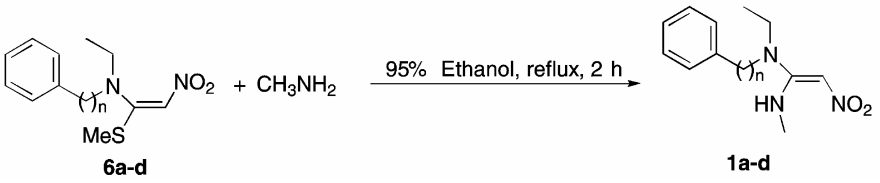
Except **6a**, in organic solvent, compounds **6b–d** exist as a sole isomer as shown by a single set of signals in the ^{13}C NMR spectra. They are probably all *(E)*-isomers because we observed a positive NOE effect between the thiomethyl group and (i) the benzylic and (ii) the vinylic hydrogen. This NOE effect is in agreement with previously reported observations concerning the 1-arylamino-1-methylthio-2-nitroethene.[19]

A further reaction between the nitroketene *S,N*-acetals **6** and two molar equivalents of aqueous solution of methylamine (40%) afforded the nitroketene aminals **1a–d** (scheme 2).

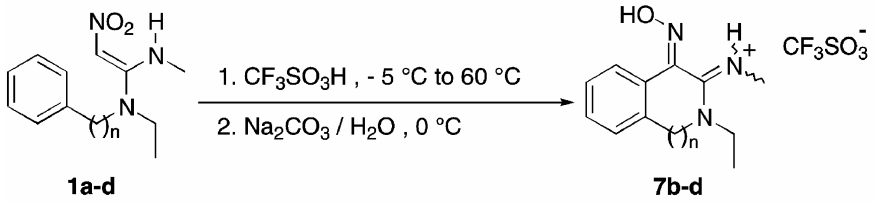
The nitroketene aminals were isolated by flash chromatography as yellow oils (eluent CH_2Cl_2/MeOH 20 : 1). The yields are reported in table 2.

Compounds **1** were mainly characterized by NMR and HRMS spectroscopy. The vinylic proton resonates in the range δ_H 6·55–6·64 ppm, the nitromethylene carbon =<u>C</u>H–NO_2 and the ><u>C</u>=C ethylene carbon close to 103·8 ppm and 163·5 ppm respectively. These chemical shifts are at higher field than those observed for the compounds **6a–d** because of the heavy atom effect of sulphur. The methylamine protons resonate in the range δ_H 2·88–3·06 ppm as a doublet because of a coupling with the amine proton ($^3J_{HH}$ 5·0–5·3 Hz) whereas their carbon resonates close to 32·6 ppm.

In organic solvent, these compounds exist as a sole isomer as shown by a single set of signals in the ^{13}C NMR spectra. They are probably all (*E*)-isomers because this conformation allows the formation of an intramolecular hydrogen bond between the N–H and one of the oxygen of the –NO_2 groups, as previ-



Scheme 2. Synthesis of nitroketene aminals **1a–d**.



Scheme 3. Synthesis of amidinium trifluoromethanesulfonates **7b–d**.

Table 2. Yields of nitroketene aminals **1a–d**.

Starting nitroketene *S,N*-acetals	**6a**	**6b**	**6c**	**6d**
Product	**1a**	**1b**	**1c**	**1d**
Yield (%)	52	56	40	36

ously reported for the 1-arylamino-1-methylthio-2-nitroethenes.[19]

2.2 *Reactions in trifluoromethanesulfonic acid*

The nitroketene aminals **1a–d** dissolved easily in triflic acid. The molar ratio trifluoromethanesulfonic acid/nitroketene aminal was 50 : 1. The reaction was carried out at 60°C under nitrogen atmosphere (scheme 3).

The starting material was fully transformed after 24 h. At the end of the reaction and after cooling, the solution was poured into 50 mL of CH_2Cl_2/MeOH (95 : 5) at –20°C. Thereafter, the resulting 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). The reaction was generally clean with yields varying from 43 to 93% (table 3) excepted for **1a** because of degradation reactions leading to the formation of dark polar products not otherwise studied.

The structures of compounds **7b–d** were determined by NMR and HRMS spectroscopy. The =N–H proton appeared as a broad singlet in the range of 9·24–9·29 ppm and the =N–OH in the range of 12·24–12·37 ppm. The C=N–H and C=N–OH carbons resonate at δ_C 146·1–147·1 ppm and 161·1–162·1 ppm respectively.

The formation of compounds **7b–d** may be explained by a similar mechanism as reported for acyclic nitroketene *S,S*-acetals[20] (scheme 4).

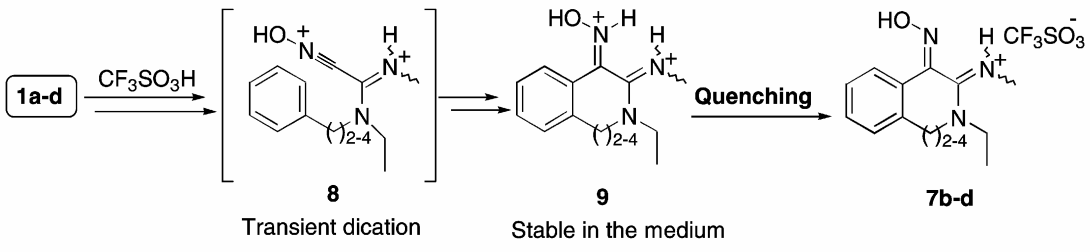
In this mechanism, the starting products **1** undergo a protonation on the carbon bearing the nitro group and an O-protonation of the nitro group. This last O-protonation occurred through a fast proton exchange process with the acidic medium, as demonstrated in fluorosulfonic acid at –80°C.[21] Prototropic exchanges and the formal loss of a molecule of water lead to the formation of the reacting conjugated hydroxynitrilium ion **8**.[20] The formation of dications **8** occurs through a rate limiting step that needs heating at 60°C, probably because the water elimination needs a further protonation to occur. In agreement with this hypothesis is the fact that with the less basic sulphur atom, formation of the stable hydroxynitrilium ions occurred even at low temperature.[20,22] As soon as it is formed, the hydroxynitrilium ion **8** reacts with the tethered phenyl ring to afford the cyclic stable doubly protonated hydroxyiminoamidine **9**.

At the end of the reaction, when the acidity was destroyed, compounds **7b–d** were isolated as triflate salts because of the strong basicity of the amidine group.[23]

3. Experimental section

3.1 *General remarks*

Melting points were determined with a Büchi Melting point B545 apparatus using capillary tubes (tem-



Scheme 4. Suggested mechanism for the formation of amidinium trifluoromethanesulfonates **7**.

Table 3. Yields of amidine triflate salts **7a–d**.

Starting compound	**1a**	**1b**	**1c**	**1d**
Amidine triflate salt	**7a**	**7b**	**7c**	**7d**
Yield (%) in recovered product	Trace	62	93	43

perature rate 2°C/mn) 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 DEPT and homo/hetero 2D techniques' and/or usual chemical shift assignments rules. – 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 to 45 μm particle size). – Trifluoromethanesulfonic acid was purchased from Across and 1,1-*bis*(methylthio)-2-nitroethene from Lancaster and were used without further purification. No special attempt was made to optimise the yields.

3.2 *1-[N-(benzyl)ethylamino]-1-methylthio-2-nitroethene (***6a***). – Typical procedure*

1,1-*bis*(methylthio)-2-nitroethene (1·82 g, 11 mmol) and the N-(benzyl)ethylamine (1·35 g, 10 mmol) were heated together in refluxing 95% ethanol (75 mL) under nitrogen atmosphere. The reaction was monitored by thin-layer chromatography (CH_2Cl_2/ethyl acetate : 20/1 and MeOH/NH_3 aq. 10/0·1). After disappearance of the N-(benzyl)ethylamine (MeOH/NH_3 aq.: 10/0·1) (6 h) the reacting medium was cooled and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent CH_2Cl_2/ethyl acetate: 20/1) to afford the oily nitroethene derivative **6a** (1·31 g, 52%) as a mixture of (Z)/(E) isomers in about 1/10 ratio. – R_f = 0·4 (CH_2Cl_2/ethyl acetate 20 : 1)) – ^{1}H NMR ($CDCl_3$, * major isomer): δ_H = 1·19 and 1·24* (*t*, 3H, *J* = 6·9 Hz, CH_2-CH_3), 2·54 and 2·54* (*s*, 3H, CH_3S), 3·56* and 4·12 (*q*, 2H, *J* = 7·0 Hz, CH_2-Me), 4·65 and 4·72* (*s*, 2 H, CH_2-Ph), 6·60 and 6·89* (*s*, 1H, vinylic H), 7·18 and 7·18* (*d*, *J* = 6·5 Hz, 2H, ar. *o*-H), 7·2–7·4 and 7·2*–7·4* (*m*, 3H, ar. *o*- and *m*-H). – ^{13}C NMR ($CDCl_3$, * major isomer): δ_C = 13·6* and 14·6 (CH_2–CH_3), 18·3* and 21·4 (SCH_3), 48·5* and 51·0 (CH_2–Me), 57·0* and 60·8 (CH_2-Ph), 112·9 and 112·9* (=CH–NO_2), 127·5 and 127·5* (ar. CH), 128·5 and 128·5* (ar. CH), 129·4 and 129·4* (ar. CH), 135·5 and 135·5* (*ipso*-C), 167·4* and 171·5 (>N–C=). – HRMS for $C_{12}H_{16}N_2O_2S$ [*M*]$^+$: calcd. 225·1517, found 225·1519 and for $C_{11}H_{13}N_2O_2S$ [M–CH_3]$^+$: calcd. 210·1283, found 210·1287.

3.3 *1-(N-ethyl-2-phenylethylamino)-1-(methylthio)-2-nitroethene (***6b***)*

From N-ethyl-2-phenylethylamine (1·49 g, 10 mmol) and 1,1-*bis*(methylthio)-2-nitroethene (1·82 g, 11 mmol) was obtained the expected nitro derivative **6b** (1·49 g, 56%) as a yellow oil. – R_f = 0·3 (CH_2Cl_2/ethyl acetate (20 : 1)) – ^{1}H NMR ($CDCl_3$): δ_H = 1·22 (*t*, 3H, *J* = 7·2 Hz, CH_2-CH_3), 2·40 (*s*, 3H, CH_3S), 2·92 (*ct*, 2H, *J* = 7·7 Hz, CH_2-Ph), 3·52 (*q*, 2H, *J* = 7·2 Hz, CH_2-Me), 3·76 (*ct*, 2H, *J* = 7·7 Hz, CH_2-N<), 6·87 (*s*, 1H, vinylic H), 7·17 – 7·36 (*m*, 5H, ar. H). – ^{13}C NMR ($CDCl_3$): δ_C = 13·5 (CH_3), 18·3 (CH_3), 34·8 (CH_2-Ph), 49·2 (CH_2-Me), 54·7 (CH_2-N), 112·4 (=CH–NO_2), 127·3 (ar. CH), 129·1 (ar. CH), 129·2 (ar. CH), 137·8 (*ipso*-C), 166·9 (–NH–C=). – HRMS for $C_{13}H_{18}NOS$ [M-NO]$^+$: calcd. 236·1109, found 236·1124.

3.4 *1-(N-ethyl-3-phenylpropylamino)-1-(methylthio)-2-nitroethene (***6c***)*

From N-ethyl-3-phenylpropylamine (1·63 g, 10 mmol) and 1,1-*bis*(methylthio)-2-nitroethene (1·82 g, 11 mmol) was obtained the expected nitro derivative **6c** (1·12 g, 40%) as a yellow oil. – R_f = 0·2 (CH_2Cl_2/ethyl acetate (30 : 1)) – ^{1}H NMR ($CDCl_3$): δ_H = 1·20 (*t*, 3H, *J* = 7·2 Hz, CH_3), 1·97 (*m*, 2H, CH_2), 2·47 (*s*, 3H, CH_3S), 2·67 (*t*, 2H, *J* = 7·6 Hz, C*H*$_2$-Ph), 3·53 (*m*, 4H, C*H*$_2$), 6·83 (*s*, 1H, vinylic H), 7·15–7·25 (*m*, 3H, ar. *o*-H and *p*-H), 7·28 (*m*, 2H, ar. *m*-H). – ^{13}C NMR ($CDCl_3$): δ_C = 13·6 (CH_3), 18·3 (SCH_3), 29·9 (CH_2), 33·1 (*C*H$_2$-Ph), 49·0 (*C*H$_2$-Me), 52·7 (CH_2-N), 111·9 (=CH–NO_2), 126·7 (ar. CH), 128·7 (ar. CH), 129·0 (ar. CH), 140·9 (*ipso*-C), 167·3 (–NH–C=). – HRMS for $C_{14}H_{20}NOS$ $[M–NO]^+$: calcd. 250·1265, found 250·1257. HRMS for $C_{14}H_{19}NS$ $[M–NO_2H]^+$: calcd. 233·1238, found 233·1244.

3.5 *1-(N-ethyl-4-phenylbutylamino) -1-(methylthio)-2-nitroethene (***6d***)*

From N-ethyl-4-phenylbutylamine (1·77 g, 10 mmol) and 1,1-*bis*(methylthio)-2-nitroethene (1·82 g, 11 mmol) was obtained the expected nitro derivative **6d** (1·06 g, 36%) as a yellow oil. R_f = 0·34 (CH_2Cl_2/ethyl acetate (30 : 1)) – ^{1}H NMR ($CDCl_3$): δ_H = 1·21 (*t*, 3H, *J* = 7·2 Hz, CH_3), 1·65 (*m*, 4H, $2CH_2$), 2·48 (*s*, 3H, CH_3S), 2·65 (*m*, 2H, C*H*$_2$-Ph), 3·50 (*ct*, 2H, *J* = 7·2 Hz, 2 CH_2), 3·52 (*q*, 2H, *J* = 7·2 Hz, C*H*$_2$-Me), 6·83 (*s*, 1H, vinylic H), 7·15–7·25 (*m*, 3H, ar. H), 7·27–7·33 (*m*, 2 H, ar. H). – ^{13}C NMR ($CDCl_3$): δ_C = 13·6 (CH_3), 18·8 (SCH_3), 27·9 (CH_2), 28·7 (CH_2), 35·8 (*C*H$_2$-Ph), 48·8 (*C*H$_2$-Me), 53·3 (CH_2-N), 111·7 (=CH–NO_2), 126·4 (ar. *C*H), 128·75 (ar. CH), 128·83 (ar. CH), 141·9 (*ipso*-C), 167·4 (–NH–C=). – HRMS for $C_{15}H_{22}NOS$ ($[M–NO]^+$): calcd. 264·1422, found 264·1407. HRMS for $C_{15}H_{22}NS$ $[M–NO_2]^+$: calcd. 248·1473, found 248·1466. HRMS for $C_{14}H_{19}N_2O_2$ $[M–SMe]^+$: calcd. 247·1447, found 247·1455.

3.6 *1-[N-(benzyl)ethylamino]-1-(methylamino)-2-nitroethene (***1a***). – Typical procedure*

1-[N-(benzyl)ethylamino]-1-(methylthio)-2-nitroethene **6a** (756 mg, 3 mmol) and the aqueous solution of methylamine (5·2 mL, 6 mmol) were heated together in refluxing 95% ethanol (25 mL) under nitrogen. The reaction was monitored by thin-layer chromatography (CH_2Cl_2/MeOH: 20/1). After disappearance of the starting compound **6a** (2 h) and cooling, the mixture was concentrated under reduced pressure and the resulting oily product was purified by flash chromatography (eluent CH_2Cl_2/MeOH (20 : 1) to afford compound **1a** (548 mg, 78%) as a yellow oil. – R_f = 0·54 (CH_2Cl_2/MeOH (20 : 1)) – ^{1}H NMR ($CDCl_3$): δ_H = 1·19 (*t*, 3H, *J* = 7·0 Hz, CH_2-C*H*$_3$), 3·06 (*d*, 3H, *J* = 5·0 Hz, CH_3-NH), 3·19 (*t*, 1H, *J* = 7·0 Hz, C*H*$_2$-Me), 4·41 (*s*, 2H, C*H*$_2$-Ph), 6·60 (*s*, 1H, vinylic H), 7·22 (*d*, 2H, *J* = 7·2 Hz, ar. *o*-H), 7·3–7·4 (*m*, 3H, ar. *p*- and *m*-H), 9·9 (*broad s*, NH). – ^{13}C NMR ($CDCl_3$): δ_C = 12·8 (CH_3), 32·7 (CH_3N), 44·7 (*C*H$_2$-Me), 53·4 (*C*H$_2$-Ph), 103·7 (=CH–NO_2), 127·6 (ar. CH), 128·4 (ar. CH), 129·4 (ar. CH), 135·8 (*ipso*-C), 163·6 (–NEt–C=). – HRMS for $C_{12}H_{17}N_3O_2$ $[M]^+$: calcd. 235·1321, found 235·1322. HRMS for $C_{12}H_{17}N_2$ $[M–NO_2]^+$: calcd. 189·1392, found 189·1398.

3.7 *1-(N-ethyl-2-phenylethylamino)-1-(methylamino)-2-nitroethene (***1b***)*

From 1-(N-ethyl-2-phenylethylamino)-1-(Methylthio)-2-nitroethene **6b** (798 mg, 3 mmol) and the aqueous solution of methylamine (5·2 mL, 6 mmol) was obtained the expected nitroethene derivative **1b** (714 mg, 96%) as yellow oil. – R_f = 0·54 (CH_2Cl_2/MeOH (20 : 1)) – ^{1}H NMR ($CDCl_3$): δ_H = 1·15 (*t*, 3H, *J* = 7·1 Hz, –CH_2–C*H*$_3$), 2·88 (*t*, 2H, *J* = 7·31 Hz, CH_2), 2·89 (*d*, 3H, *J* = 5·3 Hz, –HN-C*H*$_3$), 3·44 (*dd*, 2H, *J* = 7·2 Hz, *J* = 6·1 Hz, C*H*$_2$), 6·57 (*s*, 1H, vinylic H), 7·14–7·18 (*m*, 2H, ar. H), 7·2–7·35 (*m*, 3H, ar. H), 9·9 (*broad s*, NH). – ^{13}C NMR ($CDCl_3$): δ_C = 13·1 (CH_3), 32·6 (CH_3N), 34·2 (*C*H$_2$-Ph), 45·8 (*C*H$_2$-Me), 49·3 (CH_2), 50·9 (CH_2-N), 103·9 (=CH–NO_2), 127·3 (ar. CH), 129·0 (ar CH), 127·3 (ar. CH), 138·1 (*ipso*-C), 163·2 (–NEt–C=). – HRMS for $C_{13}H_{19}N_2O$ $[M–NO]^+$: calcd. 219·1497, found 219·1494.

3.8 *1-(N-ethyl-3-phenylpropylamino)-1-(methylamino)-2-nitroethene (***1c***)*

From 1-(N-ethyl-3-phenylpropylamino)-1-(methylthio)-2-nitroethene **6c** (840 mg, 3 mmol) and the aqueous solution of methylamine (5·2 mL, 6 mmol) was obtained the expected nitroethene derivative **1c** (747 mg, 95%) as a yellow oil. – R_f = 0·35 (CH_2Cl_2/MeOH 20 : 1). – ^{1}H NMR ($CDCl_3$): δ_H = 1·15 (*t*, 3H, *J* = 7·0 Hz, CH_3), 1·92 (*m*, 2H, *J* = 7·3 Hz, *J* = 7·5 Hz, CH_2), 2·62 (*t*, 2H, *J* = 7·3 Hz, C*H*$_2$-Ph), 2·90 (*d*, 3H, *J* = 5·1 Hz, CH_3-N), 3·17 (*t*, 2H, *J* = 7·8 Hz, CH_2-

N<), 3·23 (*q*, *J* = 7·0 Hz, CH_2-Me), 6·55 (*s*, 1H, vinylic H), 7·15 (*d*, 2H, *J* = 7·2 Hz, ar. *o*-H), 7·26 (*d*, 1H, *J* = 6.9 Hz, ar. *p*-H), 7·30 (*dd*, 2H, *J* = 6·9 Hz, *J* = 7·2 Hz, ar. *m*-H), 9·91 (*broad s*, NH). – ^{13}C NMR ($CDCl_3$): δ_C = 12·8 (CH_3), 29·0 (CH_2), 32·2 (CH_3N), 32·8 (*C*H_2-Ph), 44·8 (*C*H_2-Me), 48·7 (CH_2N), 103·3 (=CH–NO_2), 126·3 (ar. CH), 128·3 (ar. CH), 128·6 (ar. CH), 140·4 (*ipso*-C), 163·0 (–NEt–C=). – HRMS for $C_{14}H_{21}N_3O_2$ $[M]^+$: calcd. 263·1633, found 263·1613. HRMS for $C_{14}H_{21}N_2$ $[M–NO_2]^+$: calcd. 217·1704, found 217·1701.

3.9 *1-(*N*-ethyl-4-phenylbutylamino)-1-(methylamino)-2-nitroethene (***1d***)*

From 1-(*N*-ethyl-4-phenylbutylamino)-1-(Methylthio)-2-nitroethene **6d** (882 mg, 3 mmol) and the aqueous solution of methylamine (5·2 mL, 6 mmol) was obtained the expected nitroethene derivative **1d** (737 mg, 89%) as a yellow oil. – R_f = 0·36 (CH_2Cl_2/MeOH 20 : 1). – ^{1}H NMR ($CDCl_3$): δ_H = 1·16 (*t*, 3H, *J* = 7·1 Hz, CH_3), 1·61 (*m*, 2H, CH_2), 2·63 (*m*, 2H, CH_2-Ph), 2·97 (*d*, 3H, *J* = 5·3 Hz, CH_3N), 3·17 (*m*, 2H, CH_2Me), 3·22 (*q*, *J* = 7·1 Hz, 2H, CH_3-CH_2-N), 6·64 (*s*, 1H, vinylic H), 7·18 (*m*, 3H, ar. *o*- and *p*-H), 7·28 (*m*, 2H, ar. *m*-H), 9·94 (*broad s*, NH). – ^{13}C NMR ($CDCl_3$): δ_C = 13·2 (CH_3), 27·3 (CH_2), 28·9 (CH_2), 32·7 (CH_3N), 35·8 (*C*H_2-Ph), 45·1 (*C*H_2–Me), 49·6 (CH_2-N), 103·7 (=CH–NO_2), 126·4 (ar. CH), 128·7 (ar. CH), 128·9 (ar. CH), 141·9 (*ipso*-C), 163·4 (–NEt–C=). – HRMS for $C_{15}H_{23}N_3O_2$ $[M]^+$: calcd. 277·1790, found 277·1795.

3.10 *(Z)-N-[3-ethyl-1,2-dihydro-5-hydroxyimino-1*H*-benzo[d]azepin-4(3*H*)-ylidene]methylamine trifluoromethanesulfonate (***7b***) – Typical procedure*

1-(N-ethyl-2-phenylethylamino)-1-(Methylamino)-2-nitroethene **1b** (248 mg, 1 mmol) was dissolved in trifluoromethanesulfonic acid (4·4 mL, 50 mmol) at –5°C. The solution was then heated to 60°C for 24 h. After cooling the solution was poured into 50 mL of a cool (–20°C) mixture of dichloromethane/methanol (95 : 5) and the resulting mixture was then 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 layers 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 (10 : 1) to afford the triflate salt **7b** (236 mg, 62%) as white crystals. – R_f = 0·3 (CH_2Cl_2/MeOH (20 : 1)). – m.p. 191·0°C (CH_2Cl_2/MeOH (95 : 5)/petroleum ether). – ^{1}H NMR ([D_6]acetone): δ_H = 1·37 (*t*, 3H, *J* = 7·2 Hz, CH_3), 3·21 (*s*, 3H, CH_3-N), 3·28 (*m*, 1H, benzylic H), 3·43 (complex *t*, 1H, *J* ≈ 16 Hz, benzylic H), 3·84 (*m*, 2H, CH_2-Me), 3·92 (*m*, 1H, cyclic N–CH<), 4·34 (*t*, *J* = 14 Hz, 1H, cyclic N–CH<), 7·37 (*m*, 2H, ar. H), 7·47 (*m*, 1H, ar. H), 7·78 (complex *d*, *J* = 8 Hz, 1H, ar. H), 8·8 (*very broad s*, 1H, =N^+H-Me), 12·2 (*very broad s*, 1H, >=N–OH). – ^{13}C NMR ([D_6]acetone): δ_C = 12·6 (N–CH_2–*C*H_3), 32·6 (*C*H_2-Ph), 33·0 (CH_3–$^+$NH=), 46·2 (N–*C*H_2–Me), 50·5 (*cyclic* –CH_2–N), 122·4 (*q*, *J* = 318 Hz, CF_3-SO_3^-), 126·2 (*ipso*-C), 127·4 (ar. CH), 132·0 (ar. CH), 132·1 (ar. CH), 132·2 (ar. CH), 137·6 (*ipso*-C), 146·1 (>C=N–H), 162·1 (>C=N–OH). – ^{19}F NMR ([D_6]acetone): δ = –78·9 ($CF_3SO_3^-$). – MS (70 eV); *m/z* (%): 232 $[M–CF_3SO_3]^+$. – HRMS for $C_{13}H_{18}N_3O$ $[M–CF_3SO_3]^+$: calcd. 232·1450, found 232·1443.

3.11 *(Z)-N-[3-ethyl-3,4,5,6-tetrahydro-1-hydroxyiminobenzo[d]azocin-2(1*H*)-ylidene]methylamine trifluoromethanesulfonate (***7c***)*

From 1-(N-ethyl-3-phenylpropylamino)-1-(Methylamino)-2-nitroethene **1c** (262 mg, 1 mmol) was obtained the cyclic triflate salt **7c** (368 mg, 93%) as white crystals. – R_f = 0·2 (CH_2Cl_2/MeOH (20 : 1)). – m.p. 214·1°C (CH_2Cl_2/petroleum ether). – ^{1}H NMR ([D_6]acetone): δ_H = 1·42 (*t*, 3H, *J* = 7·2 Hz, CH_2-CH_3), 2·24 (*m*, 2H, CH_2), 2·93 (*m*, 2H, CH_2), 3·20 (*s*, 3H, N-CH_3), 3·83 (*q*, 2H, CH_2-CH_3), 4·08 (*t*, 2H, *J* = 6·5 Hz, –CH_2–N<), 7·40–7·55 (*m*, 3H, ar. H), 8·16 (*dd*, 1H, *J* = 3·2 Hz, *J* = 2·0 Hz, ar. H), 9·0 (*vbs*, 1H, >=NH), 12·3 (*vbs*, 1H, >=N–OH). – ^{13}C NMR ([D_6]acetone): δ_C = 11·9 (CH_3), 29·6 (CH_2), 32·7 (NH–CH_3), 32·9 (*C*H_2–), 46·3 (*C*H_2-Me), 52·4 (CH_2-N<), 122·3 (*q*, J_{CF} = 318 Hz, $CF_3SO_3^-$), 128·0 (ar. CH), 128·9 (*ipso*-C), 132·48 (ar. CH), 132·52 (ar. CH), 133·3 (ar. CH), 141·1 (*ipso*-C), 146·9 (>=N–H), 161·8 (>=N–OH). – ^{19}F NMR ([D_6]acetone): δ = –78·9 ($CF_3SO_3^-$). – MS (70 eV); *m/z* (%): 246 $[M\text{-}CF_3SO_3]^+$. – HRMS for $C_{14}H_{20}N_3O$ $[M\text{-}CF_3SO_3]^+$: calcd. 246·1606, found 246·1613.

3.12 *(Z)-*N*-[3-ethyl-4,5,6,7-tetrahydro-1-hydroxyimino-1*H*-benzo[d]azonin-2(3*H*)-ylidene]methylamine trifluoromethanesulfonate (***7d***)*

From 1-(N-ethyl-4-phenylbutylamino)-1-(Methylamino)-2-nitroethene **1d** (276 mg, 1 mmol) was obtained the cyclic triflate salt **7d** (177 mg, 43%) as

white crystals. – R_f = 0·4 (CH_2Cl_2/MeOH (10 : 1)). – m.p. 147·6°C (acetone/petroleum ether). – ^{1}H NMR ([D_6]acetone): δ_H = 1·32 (*t*, 3H, *J* = 7·2 Hz, CH_3), 1·73 (*bs*, 2H, CH_2), 2·06 (*quintuplet*, 2H, CH_2), 2·88 (*t*, 2H, *J* = 6 Hz, CH_2), 3·26 (*bs*, 3H, CH_3–N<), 3·74 (*quadruplet*, 2H, *J* = 7·2 Hz, CH_2Me), 3·78 (*bs*, 2H, –CH_2–N), 7·3–7·5 (*m*, 4H, ar. H), 9·1 (*vbs*, 1H, >=NH), 12·2 (*vbs*, 1H, >=N–OH). – ^{13}C NMR ([D_6]acetone): δ_C = 11·9 (CH_3), 29·1 (CH_2), 31·6 (*bs*, CH_2), 33·6 (CH_3-N), 47·4 (CH_2-Me), 51·5 (*bs*, –CH_2–N<), 122·3 (*q*, J_{CF} = 318 Hz, $CF_3SO_3^-$), 128·0 (ar. CH), 129·6 (*bs*, ar. CH), 130·5 (*bs*, *ipso*-C), 132·0 (ar. CH), 132·4 (ar. CH), 142·4 (*ipso*-C), 147·1 (>=N–H), 161·1 (>=N–OH). – ^{19}F NMR ([D_6]acetone): δ = –78·9 ($CF_3SO_3^-$). – MS (70 eV); *m/z* (%): 260 $[M–CF_3SO_3]^+$. – HRMS for $C_{15}H_{22}N_3O$ ($[M\text{-}CF_3SO_3]^+$): calcd. 260·1763, found 260·1754.

4. Conclusion

In the present study, the bicyclic N-(3-ethylhydrohydroxyiminobenzocycloalkenylidene) methylamine trifluoromethanesulfonates salts have been easily prepared from various 1-[N-ethyl-N-(ω-phenylalkyl) amino]-1-methylamino-2-nitroethenes in trifluoromethanesulfonic acid. Theses derivatives may be used in natural products synthesis and work in this field is in progress.

Acknowledgement

Thanks to CNRS for the financial support and to 'Ministère des Affaires Étrangères' for fellowship fund.

References

1. 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 and Taniguchi N 2000 *Biochem. Biophys. Res. Commun.* **270** 663
2. 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 and Kuo 2000 *Bioorg. Med. Chem.* **8** 601
3. Buschi C A and Pomilio A B 1987 *Phytochemistry* **26** 863
4. De la Rosa R, Martinez-Barraza V, Burgos C and Alvarez-Builla J 2000 *Tetrahedron Lett*. **41** 5837
5. Boyd G V 1991 *Reactions and synthetic uses of amidines, in the chemistry of amidines and imidates* (eds) S Patai and Z Rappoport (New York: John Wiley) vol 2, pp 367–424
6. (a) Zablocki J A, Miyano M, Garland R B, Pireh D, Schretzman L, Rao S N, Lindmark R J, Panzer-Knodle S G, Nicholson N S, Taite B B, Salyers A K, King L W, Campion J G and Feigen L P 1993 *J. Med. Chem.* **36** 1811; (b) Peterlin-Mašič L and Kikelj D 2001 *Tetrahedron* **57** 7073
7. Nishiwaki H, Nakagowa Y, Ueno T, Kagabu S and Mishimura K 2001 *Pest Manage. Sci*. **57** 810
8. Bailey C, Baku E, Hayler J and Kane P 1999 *Tetrahedron Lett*. **40** 4847
9. Stahle H 2000 *Best Practice Res. Clin. Anaesthesiol.* **14** 237
10. (a) Gauter J A, Miocque M and Farnoux C C 1975 In *The chemistry of amidines and imidates* (ed.) S Patai (New York: John Wiley) vol. 1, pp 283–348; (b) Boyd G V 1991 In *The chemistry of amidines and imidates* (eds) S Patai and Z Rappoport (New York: John Wiley) vol. 2, pp 367–424
11. Stilz H U, Jablonka B, Just M, Knoll J, Paulus E F and Zoller G 1996 *J. Med. Chem.* **39** 2118
12. Thurkauf A and Laballed J 1997 *Compd. Radiopharm*. **39** 123
13. Judkins B D, Allen D G, Cook T A, Evans B and Sardharwala T A 1996 *Synth. Commun.* **26** 4351
14. Cesar J, Nadrah K and Dolenc M S 2004 *Tetrahedron Lett.* **45** 7445
15. Gielen H, Alonso-Alija C, Hendrix M, Niewöhner U and Schauss D 2002 *Tetrahedron Lett.* **43** 419
16. Soro Y, Bamba F, Siaka S and Coustard J-M 2006 *Tetrahedron Lett.* **47** 3315
17. Rajappa S 1999 *Tetrahedron* **55** 7065
18. Pavlova Z F, Lipina E S and Perekalin V V 1995 *Sulphur Report* **16**149
19. Kearney T, Harris P A, Jackson A and Joule J A 1992 *Synthesis* **8** 769
20. Coustard J-M 2001 *Eur. J. Org. Chem*. 1525
21. (a) Olah G A and Kiovski T E 1968 *J. Am. Chem. Soc.* **90** 6461; (b) Olah G A, Fung A P and Rawdah T N 1980 *J. Org. Chem.* **45** 4149
22. (a) Coustard J-M 1999 *Tetrahedron* **55**, 5809; (b) Coustard J-M 1996 *Tetrahedron* **52** 19509
23. Häfelinger G and Kuske F K H 1991 In *The chemistry of amidine and imidate* (eds) S Patai and Z Rappoport (New York: John Wiley) pp 1–93; and references cited therein