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Reaction of 3-Amino-acridine with Formaldehyde in Acidic Medium: Influence of the Stoechiometry on the Reaction Products

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Abstract : 3-amino-acridine **1** reacts with formaldehyde in acidic medium to give four different compounds depending on the stoechiometry of the reaction: the dihydrooxazine derivative **2**, the tetrahydropyrimidine derivative **3**, the Tröger's Base analogue **4** and the acridino[3,4-j]-benzo[b][1,7]phenanthroline **5**. Compounds **3**, **4** and **5** could be obtained selectively by using the required amount of formaldehyde. Selective synthesis of **2** was independently realized in a three step sequence. Compounds **2**, **3** and **4** in solution in 12 N HCl slowly transformed to give compound **5** as a major product.

INTRODUCTION

Acridine derivatives have long been known to interact with nucleic acids[1] and to show a large variety of biological properties.[2] We were interested in modifying the 3-aminoacridine to take advantage of the intercalating properties of the acridine nucleus to bring an active group (alkylating function, chiral group, ligand for metal complexation) close to the macromolecule.

In previous work, we studied the reactivity of amino-acridines in electrophilic substitution. The H/D exchange in acidic medium occurred regioselectively on positions 4 and 5 of the proflavine (3,6-diaminoacridine) and on position 4 of the 3-aminoacridine[3]. The positions 2 and/or 7 of 3-amino or 3,6-diaminoacridines appeared totally unreactive. This observation was extended to other electrophilic reactions and was used to prepare the 10-amino-benzo[b][1,7]phenanthroline.[4] Reaction with formaldehyde in acidic media was used to prepare various polysubstituted compounds, including dihydrooxazine derivatives of interest as potential anticancer drugs[5] and Tröger's Base analogues[6], designed to achieve the chiral recognition of DNA. In the synthesis of the Tröger's Base analogues, the dihydrooxazines were obtained as side-products, along with the tetrahydropyrimidine derivatives. To rationalize this observation and selectively prepare each type of compound, we studied in detail the reaction of 3-aminoacridine **1** with formaldehyde in hydrochloric acid. Here, we present the results of our study and describe the selective synthesis of the three compounds: the dihydrooxazine **2**, the tetrahydropyrimidine **3** and the Tröger's Base **4**. We also report the formation of a new class of reaction product,

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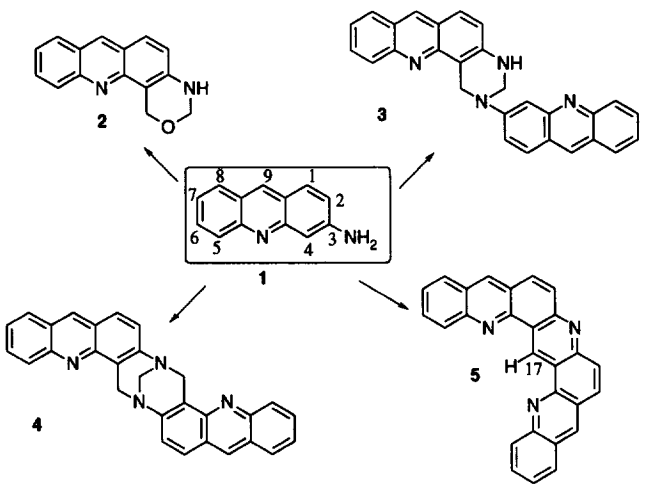
the acridino[3,4-j]benzo[b][1,7]-phenanthroline **5**. This polycyclic compound **5** appeared to be the thermodynamic compound, as products **2**, **3** and **4** transformed into **5** after prolonged acidic treatment.

RESULTS AND DISCUSSION

The reaction of formaldehyde with simple aromatic amines has been documented for many years. The nature of the reaction products depends on the nature of the acid. In formic acid, a methylation reaction occurs. This reaction is known as the Eschweiler-Clarke reaction.[7] In hydrochloric acid, formation of a Tröger's Base from *para*-toluidine was described[8]. It is interesting to note that the corresponding tetrahydropyrimidine derivative has been proposed as intermediate in the formation of the Tröger's Base.[9] We studied the reaction of **1** with formaldehyde in 6N and 12N hydrochloric acid. We used different initial concentrations of **1** and different stoechiometries of formaldehyde. Results are collected in Table 1.



Scheme 1: Compounds formed by reaction of **1** with formaldehyde in hydrochloric acid

In 6N hydrochloric acid, two compounds were formed, the dihydrooxazine **2** and the tetrahydropyrimidine **3**. Dilution of the reaction medium had little influence on the formation of dihydrooxazine **2** but decreased the yield in tetrahydropyrimidine **3**. Changes in the stoechiometry of formaldehyde had a major influence on the ratio of the two compounds. A large excess (6-20 equivalents) of formaldehyde appeared necessary to form compound **2**, and, at the opposite, compound **3** was formed in high yield when two equivalents of formaldeyde were used. In this solvent the best conditions to prepare the dihydrooxazine **2** (37 % yield) were high dilution ($3.4\ 10^{-4}$ mole.L^{-1}) and a large excess of formaldehyde (20 equivalents). For the tetrahydropyrimidine **3**, the best yield (75 %) was obtained in a more concentrated solution ($3.4\ 10^{-3}$ mole.L^{-1}) using only 2 equivalents of formaldehyde.

In 12N hydrochloric acid however, only a trace of the dihydrooxazine **2** was formed. The reactions were performed in concentrated solution (10^{-1} mole.L^{-1}). Three products were obtained selectively depending on the stoechiometry of formaldehyde: 1.5 equivalents favored the formation of the Tröger's Base analogue **4**, 1 equivalent yielded the tetrahydropyrimidine **3** and 0.5 equivalent gave a new heterocycle, acridino[3,4-j]-

benzo[b][1,7]-phenanthroline **5**. The latter reaction was very slow (two weeks at 50°C) and hplc analysis indicated that at least three unidentified intermediates were formed.

Table 1: Reactivity of 3-aminoacridine **1** with paraformaldehyde: Reaction conditions and yields determined by hplc analysis or, given in brackets, yields of the purified product.

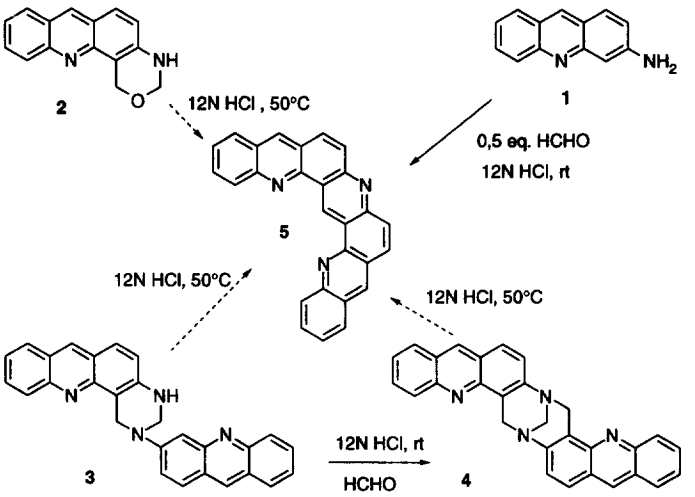
[**1**] (mol.L^{-1})[a]	$(HCHO)_n$[b]	Acid	**2** %	**3** %	**4** %	**5** %
3.4 10^{-4}	20	6N HCl	37	20	nd	nd
3.4 10^{-3}	20	"	30	50	nd	nd
3.4 10^{-3}	6	"	24	58	nd	nd
3.4 10^{-3}	2	"	7	75	nd	nd
10^{-1}	1.5	12N HCl	traces	nd	85 (68)	nd
10^{-1}	1	"	traces	90 (60)	nd	nd
10^{-1}	0.5	"	traces	nd	nd	>90 (58)[c]

Reactions were performed at room temperature a) initial concentration of compound **1**; b) stoechiometry in formaldehyde given in number of equivalents relative to **1**; c) yield obtained after two weeks of stirring at 50°C.

The four compounds (**2-5**) were easily identified by ^{1}H nmr spectroscopy. As previously published,[6a] the dihydrooxazine **2** was characterized by the presence of seven aromatic protons and by two singlets appearing at 4.90 and 5.45 ppm corresponding to the two methylene groups. The spectrum of the tetrahydropyrimidine **3** showed two sets of signals corresponding to two different acridine nuclei and two singlets at 5.11 and 5.27 ppm corresponding to the methylene groups. The Tröger's Base **4** was identified by the aromatic protons integrating for two acridine nuclei, and two AB doublets at 5.07 and 5.17 ppm respectively for the H_{endo} and H_{exo} of the benzylic methylenes and a singlet at 4.57 ppm for the methano bridge. The new heterocycle **5** showed only aromatic protons. Due to the symmetry of the molecule, all signals integrated for two protons with the exception of the singlet corresponding to the internal H-17 proton that was shifted to low fields at 11.59 ppm. The ^{13}C NMR confirmed this symmetry as the spectrum contained only fourteen peaks, including eight C-H signals as shown by a DEPT experiment. The mass spectrometry and elemental analysis were in agreement with the proposed structures.

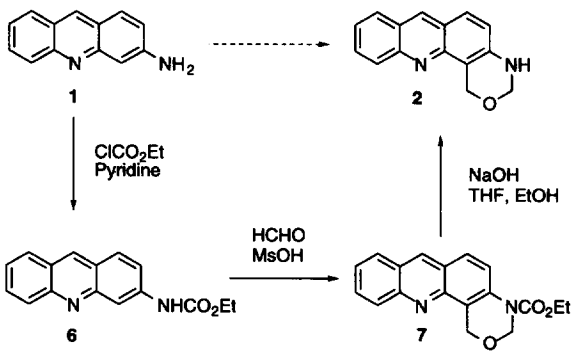
The formation of the four compounds appeared to be competitive. We thus looked for their possible interconversion. A tetrahydropyrimidine derivative has been proposed to be an intermediate in the synthesis of the original Tröger's Base derived from *para*-toluidine.[8] We have thus checked that compound **3** reacted with paraformaldehyde in 12N hydrochloric acid to give the Tröger's Base analogue **4** almost quantitatively as shown by hplc analysis. The behaviour in acidic conditions was also studied. The dihydrooxazine **2**, the tetrahydropyrimidine **3** and the Tröger's Base analogue **4** were stirred in 12N hydrochloric acid at 50°C in the absence of formaldehyde. The hplc analysis showed that, after two weeks, each compound had slowly decomposed via several unidentified intermediates to give the heptacycle **5** almost quantitatively. Compound **5**

appeared completely stable in 12N hydrochloric acid, it can be thus considered as the thermodynamic product of the reaction of 3-aminoacridine with formaldehyde.



Scheme 3

In 12N HCl, it was possible to selectively prepare the dimeric compounds **3**, **4** and **5** by using respectively 1, 1.5 and 0.5 equivalents of formaldehyde, i.e. the exact stoechiometry required for each compound. The yield of formation of the dihydrooxazine **2** could not be improved, compounds **3** and **4** being also always produced. To selectively prepare this interesting compound, we designed a three step synthesis (Scheme 4).



Scheme 4

3-aminoacridine **1** was monoprotected with ethyl chloroformate to yield compound **6** in 84 %. The carbamate **6** thus formed reacted with a large excess of paraformaldehyde in methane sulfonic acid to give the carbamate substituted dihydrooxazine **7** in 68 % yield. The cyclisation occurred in methane sulfonic acid, while no reaction was observed in 12N hydrochloric acid. The hydrolysis of compound **7** in basic conditions gave the dihydrooxazine **2** in 83 % yield. Compound **2** was thus synthesized in three steps with 47% overall yield.

CONCLUSION

Condensation of the 3-amino-acridine **1** with formaldehyde in hydrochloric acid is a very versatile reaction. Several pathways are competitive and depending on the strength of the acid (6N or 12N hydrochloric acid) and on the stoechiometry of formaldehyde, four different types of compounds could be prepared: a dihydrooxazine **2**, a tetrahydropyrimidine **3**, a Tröger's Base **4** and an heptacyclic heteroaromatic compound **5**. Using the exact stoechiometry required for their formation (1, 1.5 and 0.5 equivalents of paraformaldehyde), compounds **3**, **4** and **5** respectively could be formed selectively in yields close to 80 % as shown by the hplc analysis (60-70 % isolated yields). To prepare **2**, a three step process was designed, including monoprotection of the amino group to prevent any bis reaction on this position. We have also shown that the heptacyclic compound **5** was stable in 12N hydrochloric acid and that it could be considered as the thermodynamic reaction product. The three other products, **2**, **3** and **4** slowly decomposed under heating in 12N hydrochloric acid to give compound **5**. Several mechanisms can explain the formation of the different products, all of them involving regioselective electrophilic substitution on position 4 (*ortho* to the amino group). The interconversion implies a dehydroalkylation.

It is worth noting that three of the reaction products have interesting properties. If Tröger's Base analogues have been extensively studied by us[6] and others,[10] dihydrooxazine derivatives have never been mentioned in the literature as being produced by reaction of aromatic amines with formaldehyde. The dihydrooxazine **2** is a precursor of *ortho*-hydroxymethylated amines of pharmaceutical interest.[5] We are currently studying their chemical reactivity. The Tröger's Base **4** is a chiral molecule that can be used in the recognition of DNA conformations[11,12]. Finally, the heptacyclic compound **5** has never been described, only partially hydrogenated analogues have been published.[13] Its method of preparation was used to prepare the 3,9,15,19,21,23-hexaazakekulene.[11]

EXPERIMENTAL

General

Melting points were determined on a Totolli melting point apparatus and were uncorrected. IR spectra were taken with Perkin Elmer 298 and 1320 spectrometers. ^{1}H NMR spectra were recorded on Bruker AC200 (200 MHz) and AM300 (300 MHz) spectrometers. Chemical shifts were expressed in parts per million, solvents used as internal standards ($CDCl_3$: 7.24 ppm; DMSO-d6: 2.49 ppm). The mass spectra (MS) were taken on a Delsi NERMAG R10-10. UV spectra were taken with a Perkin Elmer Lambda UV-visible spectrophotometer. Elemental analyses were performed at the "Laboratoire Central d'Analyse"—CNRS (Lyon). Thin-layer chromatography (TLC) was done on Merck Kieselgel F-254 precoated plates. Visualization was made with ultraviolet light (254 and 365 nm). For preparative column chromatography, silica gel 60 Merck (230-240 mesh ASTM) was used. High performance liquid chromatography (HPLC) was performed on a Waters equipment (two M-510 pumps, solvent gradient M-680) with UV detection (diode array detector 990). Reversed phase μ-bondapak C-18 (Waters) was used with methanol-water pH 2.5 (phosphoric acid) gradient, flow rate 2 mL/min. All reagents were purchased from Aldrich Chimie and used without further purification.

2-(acridin-3-yl)-1,2,3,4-tetrahydropyrimidino[4,5-c]acridine 3

3-amino-acridine **1** (1 g ; 5.15 mmol) and a stoechiometric amount of paraformaldehyde (154 mg ; 5.13 mmol) were dissolved in 10 cm^3 of 12N HCl . A precipitate appeared immediately and 10 cm^3 of 12N HCl was added to the solution and then stirred for 1 h. The solution was then basified with diluted aqueous ammonium hydroxide and extracted with ethyl acetate (5 x 300 cm^3). The organic layer was washed with distilled water, dried over sodium sulfate and evaporated until precipitation. Tetrahydropyrimidine **3** (644 mg ; 1.56 mmol) was collected by filtration in 60% yield (recrystallized in methanol as an hydrochloride for analysis), F = 175-178°C. ^{1}H-NMR (300 MHz, DMSO-d_6): δppm = 8.85 (1H, s, H-7 or H-9') ; 8.76 (1H, s, H-9' or H-7) ; 8.10 (1H, d, J = 8.5Hz) ; 8.04-8.00 (2H, with H-1' at 8.02 ppm) ; 7.92 (1H, d, J = 8.5Hz) ; 7.79-7.68 (5H, m, with H-6 at 7.78 ppm and H-2' at 7.75 ppm) ; 7.48-7.41 (2H, m) ; 7.36 (1H, s, H-4') ; 7.25 (1H, s, N-H) ; 7.03 (1H, d, J = 9Hz, H-5) ; 5.27 (2H, s, Ar-CH_2-N) ; 5.11 (2H, s, N-CH_2-N). MS (DCI) : M = 412, m/z : 413 (100, $[M+H]^+$). UV (Ethanol) : λmax (ε) : 417 (11000) ; 356 (1200) ; 340 (9100) ; 278 (63000) ; 271 (62000) ; 241 (62400) nm. IR (KBr) : 3400, 3200, 1630, 1610, 1520, 1490, 1450, 1430, 1400, 1360, 1330, 1270, 1240, 1170, 1130, 1010, 990, 970, 910, 850, 820, 790, 745, 735 cm^{-1}. Anal. : Found.: C-74.51, H-4.81, N-12.07 ; Calcd. for $C_{28}H_{20}N_4$ + HCl + 0.25 H_2O: C-74.23, H-4.79, N-12.37.

9H,19H-10,20-methanodiacridino[3,4-b:3',4'-f][1,5]diazocine 4

Method A: To the 3-aminoacridine hydrochloride **1** (0.21 g, 0.9 mmol) dissolved in 12N hydrochloric acid (3 cm^3) was added one equivalent of paraformaldehyde (0.031 g, 1.03 mmol) and the resulting solution was stirred at room temperature for 40 min. A green-yellow precipitate, corresponding to the tetrahydropyrimidine derivative **3**, was formed. An excess of formaldehyde (0.062 g, 2.06 mmol) suspended in 12N hydrochloric acid (4 cm^3) was then added to the solution and the mixture was stirred again at room temperature for 22 h. As shown by hplc analysis, Tröger's Base **4** was formed in 90 % yield. The solution was then neutralized with aqueous ammonium hydroxide and extracted with methylene chloride. Compound **4** was purified by column chromatography (SiO_2, eluted with ethylacetate-chloroform mixture). The product was isolated in 60 % yield (0.12 g, 0.27 mmol).

Method B: A mixture of 3-aminoacridine hydrochloride **1** (1.08 g, 4.68 mmol) and paraformaldehyde (0.25 g, 8.3 mmol) in HCl 12N (15 cm^3) was stirred at room temperature for 2 h. The reaction mixture was then basified with aqueous ammonium hydroxide and extracted with methylene chloride. The organic layers were collected, washed with water and evaporated to dryness. The solid residue was triturated in the minimum amount of methanol and filtered. Tröger's Base **4** was obtained with 68 % yield (0.684 g, 1.6 mmol). F = 350°C. NMR^{1}H (200 MHz, $CDCl_3$) : δppm = 8.48 (2H, s, H-10,20) ; 8.1 (2H, d, J = 5.8Hz, H-4,14) ; 7.82 (2H, d, J = 5.5Hz, H-1,11) ; 7.66 (4H, m, H-9,19 and H-3,13) ; 7.4 (4H, m, H-8,18 and H-2,12) ; 5.17 (2H, d, J = 16.8Hz, 2Ar-$\underline{CH_2}$-N*endo*) ; 5.07 (2H, d, J = 16.5Hz, 2Ar-$\underline{CH_2}$-N*exo*) ; 4.57 (2H, s, N-$\underline{CH_2}$-N). MS (FAB(+)) : M = 424, m/z = 425 $[M+H]^+$. UV (Ethanol) : λ_{max} (ε) : 358 (15550) ; 265 (72600) ; 247 (81700) ; 209 (108130) nm. IR (KBr) : 3050, 3015, 2965, 1620, 1610, 1555, 1515, 1475, 1455, 1435, 1405, 1340, 1295, 1260, 1250, 1205, 1170, 1160, 1130, 1090, 1080, 1065, 1020, 980, 945, 930, 910, 850, 825, 735, 665 cm^{-1}. Anal. : Found. : C-81.51, H-4.75, N-13.09 ; Calcd. for $C_{29}H_{20}N_4$: C-82.05, H-4.75, N-13.2.

acridino[3,4-j]benzo[b][1,7]phenanthroline 5.

3-amino-acridine hydrochloride **1** (132 mg, 0.57 mmol) and paraformaldehyde (8.6 mg, 0.29 mmol) were solubilized in 12N HCl (10 cm^3). The mixture was stirred for two weeks at 50°C. After cooling to room

temperature, the solution was basified with aqueous ammonium hydroxide and extracted with ethylacetate (5 x 200 cm^3). The organic layers were collected, washed with water (2 x 100 cm^3), dried over sodium sulfate and evaporated to dryness. The crude product was dissolved in dimethylformamide with a few drops of 12N HCl and precipitated with acetone to give the heptacyclic compound **5** (72 mg ; 0.165 mmol) in 58 % yield, F = 305-310°C. ^{1}H-NMR (300 MHz, $CDCl_3$) : δppm = 11.59 (1H, s, H-17) ; 8.69 (2H, s, H-5,11) ; 8.58 (2H, d, J = 8.6Hz, H-4,12) ; 8.06 (6H, m, H-6,10, H-7,9, H-1,15) ; 7.90 (2H, m, H-3,13) ; 7.65 (2H, m, H-2,14). ^{13}C-NMR (300MHz, $CDCl_3$) : δ ppm = 151.5 ; 148.1 ; 147.6 ; 135.3 (CH) ; 131.3 (CH) ; 131.1 (CH) ; 130.2 (CH) ; 130.1 (CH) ; 128.8 (CH) ; 128 (CH) ; 127.3 ; 126.5 (CH) ; 126.1 ; 124.7. MS (FAB(+)) : M = 381, m/z : 382 $[M+H]^+$. UV (Ethanol) : λmax(ε) : 365 (29300) ; 336 (73700) ; 268 (36700) ; 246 (95500) nm. IR (KBr) : 3050, 1600, 1560, 1480, 1430, 1380, 905, 825, 740, 695 cm^{-1}. Anal. : Found: C-74.65, H-3.42, N-9.48 ; Calcd. for $C_{27}H_{15}N_3$ + 1.5 HCl : C-74.36, H-3.81, N-9.63.

3-ethoxycarbonylamino-acridine 6

3-amino-acridine **1** (2.5 g ; 12,9 mmol) was dissolved in 22 cm^3 of pyridine. The solution was cooled to 0°C, and ethyl chloroformate (1.84 cm^3; 19.2 mmol) was added by portions. The mixture was stirred for 30 min at 0°C and one night at room temperature. The mixture was then diluted with 170 cm^3 of water and stirred for 1 h. The resulting solid was collected by filtration, washed with water and diethylether and dried at 40°C under reduced pressure. Compound **6** (2.88 g ; 10.85 mmol) was obtained in 80% yield. F = 180°C. ^{1}H-NMR (200 MHz, DMSO-d_6) : δppm = 10.14 (1H, s, N-H) ; 8.95 (1H, s, H-9) ; 8.32 (2H, d, J = 1.8Hz, H-4) ; 8.07 (1H, d, J = 9.1Hz, H-1) ; 8.12-8.05 (2H, H-5 et H-8) ; 7.79 (1H, dd, J = 8.6Hz and J = 7Hz, H-7 or H-6) ; 7.64 (1H, dd, J = 9.1Hz and J = 1.8Hz, H-2) ; 7,53 (1H, dd, J = 8.6Hz and J = 7Hz, H-6 or H-7) ; 4,21 (2H, q, J = 7.1Hz, CH_2) ; 1,29 (3H, t, J = 7.1 Hz, CH_3). MS (EI) : M = 266, m/z : 267 (100, $[M+H]^+$), 238 (1, $[M-C_2H_5]^+$), 220 (3, $[M-C_2H_5OH]^+$), 194 (3, $[M-(C_2H_4+CO_2)]^+$). UV (Ethanol) : λmax(ε) : 384 (6750) ; 356 (8870) ; 339 (5670) ; 264 (94600) ; 231 (32700) nm. IR (KBr) : 3020, 3010, 2950, 1725, 1640, 1490, 1430, 1305, 1235, 1210, 1170, 1095, 1060, 910, 775 cm^{-1}. Anal. : Found: C-71.09, H-5.21, N-10.38 ; Calcd. for $C_{16}H_{14}N_2O_2$ + 0.5 H_2O : C-69.8, H-5.45, N-10.18.

4-ethoxycarbonyl-3,4-dihydro-1H-[1,3]oxazino[4,5-c]acridine 7

Compound **6** (2.72 g ; 10.2 mmol) was solubilized in methane sulfonic acid (27 cm^3) in the presence of 37% aqueous formaldehyde (2.7 cm^3). The solution was stirred at 28 °C and sonicated. After 15 h, the mixture was poured slowly in a solution of ice, aqueous ammonium hydroxide and ethyl acetate (100 cm^3/40 cm^3/230 cm^3). The aqueous phase was separated and extracted again with 100 cm^3 of ethyl acetate. The organic layers were collected, dried over sodium sulfate and evaporated to dryness under reduced pressure. The crude product was chromatographied on silica gel with chloroform/acetonitrile (98/2). The protected dihydrooxazine **7** (2.2 g ; 7.3 mmol) was obtained in 68 % yield. F = 97-98°C. ^{1}H-NMR (200 MHz, $DMSOd_6$) : δppm = 9.06 (1H, s, H-17) ; 8.18-7.58 (6H, m, H-5, H-6, H-8, H-9, H-10, and H-11) ; 5.50 (2H, s, Ar-CH_2-O) ; 5.29 (2H, s, O-CH_2-N) ; 4.27 (2H, q, J = 7.04 Hz, CO_2-CH_2) ; 1.31 (3H, t, J = 7.04Hz, CH_3). ^{13}C-NMR (200MHz, $CDCl_3$) : δ ppm = 154.9 (CO) ; 149.5 ; 146.9 ; 139.9 ; 136.4 ; 131.0 ; 128.9 ; 127.0 ; 124.2 ; 124.0 ; 122.2 ; 75.6 ; 66.9 ; 63.0 (CO_2-CH_2) ; 14.5 (CH_3). MS (DCI) : M = 308, m/z : 309 (100, $[M+H]^+$), 279 (13, $[M- CH_2CH_3]^+$), 235 (12, $[M-CO_2Et]^+$). UV (Ethanol) : λmax(ε) : 360 (10200) ; 263 (85000) nm. IR (KBr) : 3900, 3850, 3005, 3000,

1726, 1471, 1408, 1373, 1298, 1273, 1228, 1194, 1136, 1088, 1037, 925, 756 cm^{-1}. Anal. : Found: C-69.57, H-5.23, N-9.05 ; Calcd. for $C_{18}H_{16}N_2O_3$: C-70.10, H-5.20, N-9.00.

3,4-dihydro-1H-[1,3]oxazino[4,5-c]acridine 2

Compound **7** (1.5g ; 4,8 mmol) was stirred at 60°C in a solution of tetrahydrofuran (40 cm^3), ethanol (20 cm^3), water (2 cm^3) and sodium 30% hydroxide (1 cm^3) for 5.5 h. An excess of water (0.5 cm^3) and 30% sodium hydroxide (0.4 cm^3) was added. The insoluble part was removed by filtration and the filtrate evaporated to dryness. The crude product was triturated with 2 cm^3 of ethanol and 20 cm^3 of diethylether. Dihydrooxazine **2** (0.88 g ; 4 mmol) was obtained with 83% yield. F = 180°C. ^{1}H-NMR (200 MHz, $CDCl_3$) : δppm = 8.65 (1H, s, H-7) ; 8.05 (1H, dd, J = 8.6Hz and J = 2Hz, H-11) ; 7.85 (1H, d, J = 8.4Hz, H-8) ; 7.65 (1H, d, J = 9Hz, H-6) ; 7.60 (1H, dd, J = 8.6Hz and J = 6.6Hz, H-10) ; 7.40 (1H, ddd, J = 8.4Hz and J = 6.6 Hz and J = 2Hz, H-9) ; 6.9 (1H, d, J = 9Hz, H-5) ; 5,45 (2H, s, Ar-CH_2-O) ; 4.9 (2H, s, O-CH_2-N) ; 4.5 (1H, s, NH). MS (FAB(+)) : M = 236, m/z : 236 $[M+H]^+$. UV (Ethanol) : λmax(ε) : 418 (5300) ; 354 (6100) ; 273 (52200) ; 240 (32800) nm. IR (KBr) : 3300, 3040, 2840, 1630, 1610, 1520, 1480, 1450, 1400, 1280, 1240, 1160, 1080, 1050, 1030, 975, 915, 885, 840, 820, 790, 735, 685, 610 cm^{-1}. Anal. : Found: C-76.1, H-5.07, N-11.6 ; Calcd. for $C_{15}H_{12}N_2O$: C-76.25, H-5.12, N-11.86.

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