Novel trichloroindolizine derivatives *via* intramolecular acylation of a bis(chloroacyl)bipyridine

Najat Sam,[a] Sghir Elkadiri,[a] Hubert Le Bozec,[b] Loic Toupet,[c] Maria Daoudi,[d] Najib Bitit,[d] Taibi Ben Hadda *[a] and Pierre H. Dixneuf *[b]

[a] *Laboratoire d'activation Moléculaire, Faculté des Sciences d'Oujda, Université Mohamed 1^er^, 60000 Oujda, Morocco. E-mail: benhadda@sciences.univ-oujda.ac.ma*
[b] *Institut de Chimie de Rennes, UMR 6509 CNRS-Université de Rennes 1, Organométalliques et Catalyse: Chimie et Electrochimie Moléculaires, Campus de Beaulieu, 35042 Rennes Cedex, France. E-mail: dixneuf@univ-rennes1.fr*
[c] *UMR CNRS 6626, Groupe de la Matière condensée et Matériaux, Campus de Beaulieu, 35042 Rennes Cedex, France*
[d] *Faculté des Sciences Dhar El Mehraz, Département de Chimie, 30000 Fès, Morocco*

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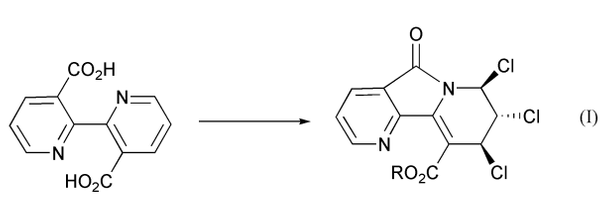
3,3′-Bis(alkyloxycarbonyl)-2,2′-bipyridines are produced from the reaction of alcohols with 3,3′-bis(chlorocarbonyl)-2,2′-bipyridine which is generated from the corresponding dicarboxylic acid and thionyl chloride. When the dicarboxylic acid is reacted with a $SOCl_2$–Cl_2 mixture, significant amounts of trichloroindolizines are produced. This reaction is likely to take place *via* initial intramolecular *N*-chloroacylation of bipyridine **3**.

Introduction

Polyfunctional indolizine derivatives have recently attracted interest due to their biological activity,[1] especially in the field of agrochemicals[2] and as anticancer and antiviral agents.[3] Functionalised indolizines are usually obtained *via* initial alkylation of a pyridine nitrogen atom, for example by 1,3-dipolar additions to pyridinium *N*-ylides,[4] or *via* initial addition of chloro carbenes.[5] We report herein the formation of new trichloroindolizine derivatives of type **I** which were also formed during our attempts to produce 3,3′-diester-2,2′-bipyridines from 2,2′-bipyridine-3,3′-dicarboxylic acids. These additional products are a result of 3,3′-bis(chlorocarbonyl)-2,2′-bipyridine reacting with the diacid and a mixture of thionyl chloride and chlorine *via* acylation of one pyridine nitrogen atom, and chlorination of the neighbouring double bond. This new two step reaction offers potential access to a variety of indolizines. The initial chloroacylation is in contrast to the usual intramolecular *C*-acylations for this class of compound as illustrated by the *C*-acylation occurring in the formation of 4,5-diazafluoren-9-one; a by-product in the synthesis of the same 2,2′-bipyridine-3,3′-dicarboxylic acid.[6]



(I)

Results and discussion

Synthesis

The diesters **4** are key starting molecules for the building of 3,3′-disubstituted-2,2′-bipyridine metal complexes.[7] Modification of the initial procedure in order to directly produce the diesters **4** from the diacid precursors **2** and thionyl chloride in the presence of alcohols[7,8] was considered. The 2,2′-bipyridine-3,3′-dicarboxylic acid **2**, prepared in 67% yield by oxidation of 1,10-phenanthroline **1** with aqueous alkaline potassium permanganate,[8] was first reacted with a large excess of old thionyl chloride containing chlorine at reflux for 5 h in an attempt to generate the diacyl dichloride derivative **3** (Scheme 1).

Excess thionyl chloride was eliminated under vacuum to afford a yellow residue which was dissolved in toluene before the addition of methanol. The mixture was refluxed for 3 h in order to produce the diester **4a**. Chromatography on silica with petroleum ether–dichloromethane separated **5a** (31%), **6a** (7%) and the diester **4a** (52%) successively, as white solids (Scheme 1). Analogously, the same intermediate, obtained from **2** and $SOCl_2$ was reacted with ethanol which led to the formation of **5b** (13%), **6b** (5%) and **4b** (83%). When the same reaction was performed after reflux in isobutanol, chromatography also afforded **5c** (16%), **6c** (6%) and **4c** (79%) (Scheme 1). The structures of compounds **4**–**6** have been established on the basis of elemental analysis, IR, NMR spectroscopy and on an X-ray diffraction study of **5b**. The IR and NMR spectra of diesters **4** correspond to those of diacid **2** and of related diesters.[8] The elemental analyses and mass spectra of derivatives **5**and **6** are consistent with a reaction resulting from one acylation and the addition of three chlorine atoms. The ^{1}H NMR spectra of compounds **5** and **6** show a typical array of signals for the consecutive protons of a disubstituted pyridine ring [H_2 (d), H_3 (dd), H_4 (d); see Chart 1 for NMR assignments]. The protons at higher field for **5a** show very small vicinal coupling constants, typical of axial–equatorial or equatorial–equatorial positions,[9] and thus indicate a consecutive *trans–trans* configuration for the chlorine atoms (Table 1). The spectra of derivatives **5b** and **5c** show similar sets of signals to **5a**. The spectrum of **6a** also shows similar signals to **5a** but with significantly larger *J* values (Table 1), thus consistent with axial–axial (^3J = 9.8 Hz) and axial–equatorial (^3J = 3.1 Hz) couplings.[9] The 2D {^{13}C–^{1}H CORR} spectrum of **5b** has enabled the correlation of each

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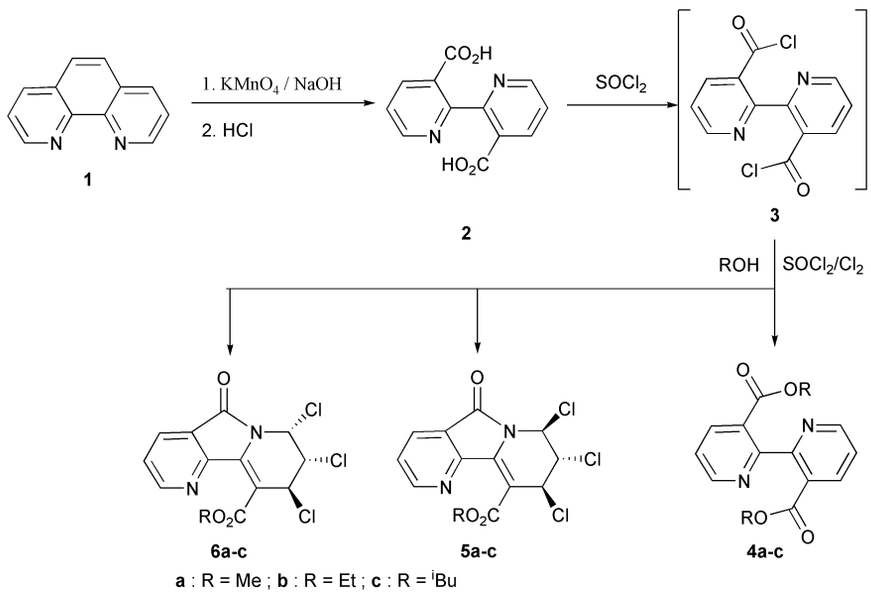
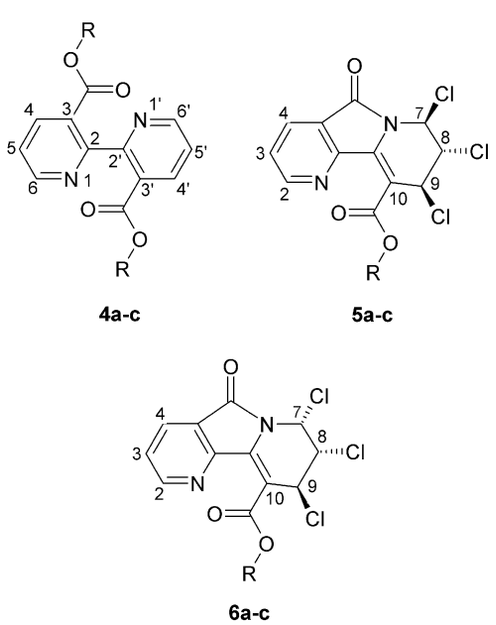
Table 1 Comparison of *J* values for derivatives **5a** and **6a**

	δ H_7 (ppm) [^3J, ^4J/Hz]	δ H_8 (ppm) [^3J/Hz]	δ H_9 (ppm) [^3J/Hz]
5a	6.49 (dd) [1.33, 2.1]	5.35 (t) [1.33]	5.03 (dd) [1.33, 2.1]
6a	6.47 (d) [3.0]	4.52 (dd) [3.0, 9.8]	5.26 (d) [9.8]



Scheme 1



a (R = Me); **b** (R = Et); **c** (R = i-Bu)

Chart 1 Labelling used for NMR assignments.

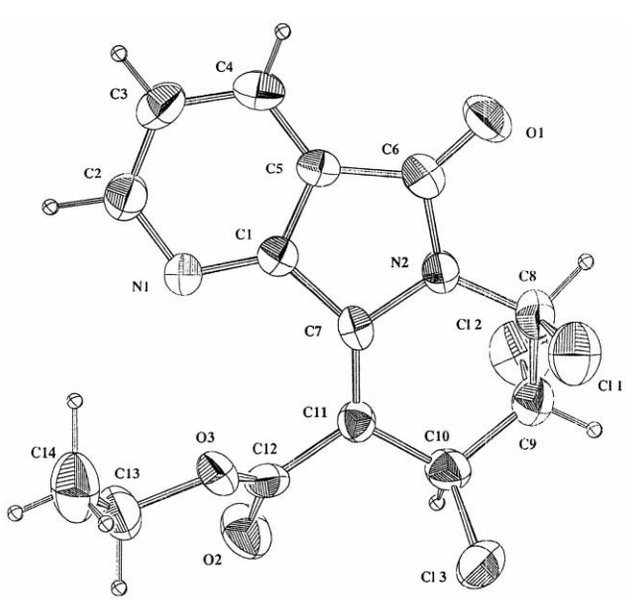


Fig. 1 X-Ray crystal structure of **5b**.

proton to each carbon nucleus of molecule **5b**. The structure of **5b** was further confirmed by an X-ray diffraction study.

X-Ray diffraction study

The structure of derivative **5b** was determined by an X-ray diffraction study (Fig. 1, Tables 2 and 3). This confirms that one pyridine ring remains unchanged while the other pyridine nitrogen atom has been acylated. Moreover, it shows that the ring containing the acylated nitrogen has been trichlorinated at consecutive carbon atoms C(7), C(8) and C(9) in a relative *trans–trans* configuration as shown in Scheme 1. The carbon atom C(8) stays above the average plane *ca.* N(2)–C(7)/C(10)–C(9). The carboxylate group is linked to carbon atom C(11).

Acylation–chlorination mechanism

Formation of the trichlorinated indolizines may be rationalized as shown in Scheme 2 by the initial formation of the expected bis(acyl chloride) **3**. A subsequent intramolecular acylation of one pyridine nitrogen atom could give access to the cation **b** which, after addition of Cl^- could afford the neutral intermediates **c** and **c′**. The next step is expected to be a classical chlorination of a double bond which preferentially gives the *trans* intermediate **d** rather than the *cis* intermediate **f**. *Trans* addition of Cl^- to the chloronium ion **d** would preferentially produce the acyl chloride **e**, the precursor of **5** and not the *cis* derivative **g**, the precursor of **6**.

According to the proposed mechanism, the presence of Cl_2 is needed to explain the unexpected formation of **5** and **6**. This was further confirmed by carrying out the following experiments: the use of freshly distilled thionyl chloride in the presence of ethanol gave the diester **4b** in 87% yield with only traces of compounds **5b** (5%) and **6b** (2%), whereas upon bubbling Cl_2 gas into the precedent mixture considerably increased yields of **5b** (45%) and **6b** (12%) were observed at the expense of **4b** (39%).

Table 2 Crystallographic data for **5b**

Formula	$C_{14}H_{11}N_2O_3Cl_3$
MW/g mol^{-1}	361.61
Crystal system	Monoclinic
Space group	$P2_1/a$
a/Å	13.536(2)
b/Å	7.787(1)
c/Å	14.769(2)
α/°	90
β/°	97.62(1)
γ/°	90
Volume/Å^3	1543.0(5)
Z	4
μ/cm^{-1}	6.067
ρ_{calc}/g cm^{-3}	1.557
Crystal size/mm	0.35 × 0.25 × 0.20
T/K	294
$2\theta_{max}$/°	54
Reflections measured	3942
Reflections observed ($I > \sigma(I)$)	2347
R	0.057
R_w	0.1699
S_w	1.094
Max residual (e Å^{-3})	0.37

Conclusion

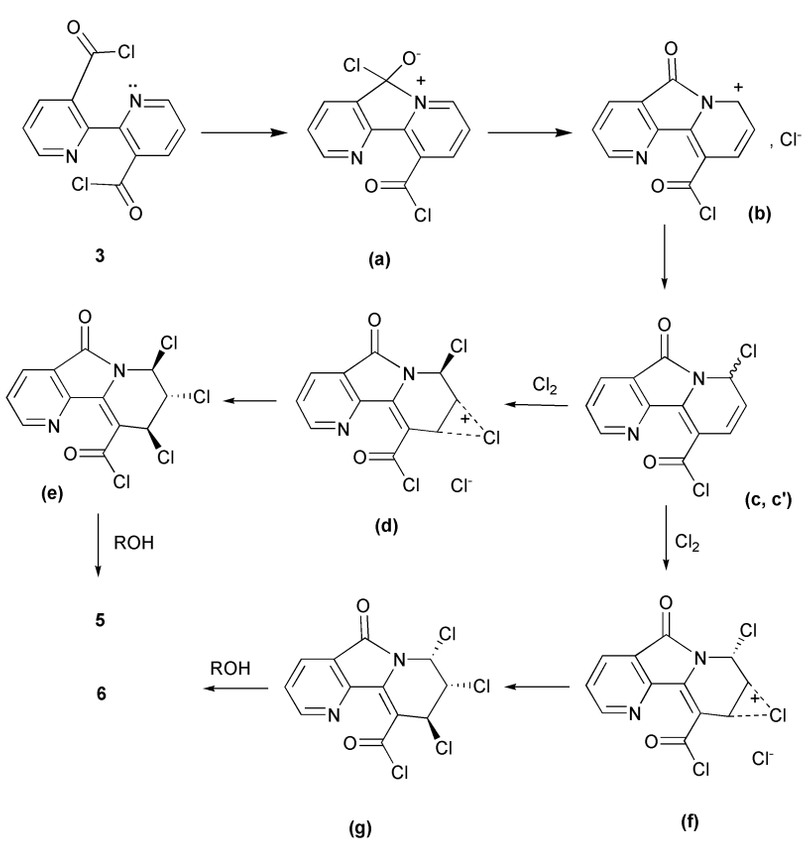
The above results show, due to the unexpected presence of chlorine in thionyl chloride, a novel transformation of 3,3′-diacid-2,2′-bipyridine into new, highly chlorinated indolizines. The mechanism suggests an initial intramolecular chloroacylation of the diacyl dichloride affording the intermediates **b** and **c**, with chlorination of **c**.These key, two step reactions, offer potential for the design of novel indolizines.

Experimental

The 3,3′-bis(hydroxycarbonyl)-2,2′-bipyridine **2** used in this work was prepared from 1,10-phenanthroline **1** by a procedure described previously.[8] ^{1}H and ^{13}C NMR spectra were recorded on a Bruker WP-80 operating at 200.131 MHz, an AC 250 at 250.14 MHz or an AM 300 at 300.134 MHz. Mass spectra (electrospray) were recorded on a Platform II Micro Mass

Table 3 Selected bond distances and bond angles for **5b**

Bond lengths/Å				Bond angles/°	
C1–C7	1.480(5)	Cl1–C8	1.810(4)	C6–N2–C8	124.5(3)
N1–C1	1.325(4)	C8–C9	1.515(5)	Cl1–C8–N2	110.7(3)
C1–C5	1.387(5)	Cl2–C9	1.785(4)	Cl1–C8–C9	110.2(3)
C5–C6	1.471(5)	C9–C10	1.533(5)	Cl2–C9–C8	107.0(3)
O1–C6	1.211(4)	Cl3–C10	1.811(4)	Cl2–C9–C10	107.5(3)
N2–C6	1.392(5)	C10–C11	1.494(5)	Cl3–C10–C9	111.3(3)
N2–C7	1.406(4)	C11–C12	1.489(5)	Cl3–C10–C11	110.0(3)
N2–C8	1.418(5)	C12–O3	1.325(5)	C10–C11–C12	116.4(3)
				C7–C11–C10	121.0(3)



Scheme 2

spectrometer, and FTIR spectra were measured on a Nicolet 205 spectrometer.

Crystallography

Crystal data and refinement details for derivative **5b** are presented in Table 1. All measurements were made on an automatic diffractometer CAD4 NONIUS with graphite monochromatized Mo-Kα radiation.[10] The data collection ($2\theta_{max}$ = 54°, scan $\omega/2\theta$ = 1, t_{max} = 60 s, range *hkl*: *h* 0.17, *k* 0.9, *l* −18.18) gives 3749 unique reflections from which 1614 with $I > 3.0\ \sigma(I)$ were considered reliable. After Lorentz and polarization corrections,[11] the structure was solved with SIR-97[12] which reveals the non-hydrogen atoms. After anisotropic refinement, all the hydrogen atoms were found with a Fourier difference. The whole structure was refined with SHELXL 97[13] by the full-matrix least-square techniques with the resulting $R = 0.052$, $R_w = 0.047$ and $S_w = 1.24$ (residual $\Delta\rho = 0.32$ e A^{-3}). Atomic scattering factors were obtained from International Tables[14] and ORTEP views realized with PLATON 98.[15] CCDC reference number 181455. See http://www.rsc.org/suppdata/p1/b2/b202616n/ for crystallographic files in .cif or other electronic format.

Synthesis of 3,3′-bis(alkoxycarbonyl)-2,2′-bipyridine (4) and alkyl 7,8,9-trichloro-5-oxo-5,7,8,9-tetrahydropyrido[2,3-*a*]-indolizine-10-carboxylates (5 and 6)

General procedure. To 10 mL of thionyl chloride, was added 600 mg (2.5 mmol) of 3,3′-bis(hydroxycarbonyl)-2,2′-bipyridine **2** and the mixture was refluxed for 5 h. The excess $SOCl_2$ was removed under vacuum to leave a yellow residue. Toluene (20 mL) and then alcohol (ROH, 1 mL) were added and the solution was heated at reflux for 3 h. Chloroform (40 mL) was added and the organic phase was washed with a cooled solution of sodium hydrogencarbonate (2.5%), and dried on sodium sulfate. The crude product was chromatographed on a silica column (*l* = 30 cm, id = 3 cm) and three white solids were successively obtained: a mixture of petroleum ether–dichloromethane (10 : 90) eluted **5** first and then, in a ratio of 5 : 95, **6** was recovered. The diester **4** was extracted by elution with ether–acetone (40 : 60).

1. With ROH = methanol: **5a** (310 mg, 31%), **6a** (70 mg, 7%) and **4a** (450 mg, 52%) were obtained.

2. With ROH = ethanol: **5b** (115 mg, 13%), **6b** (46 mg, 5%) and **4b** (668 mg, 80%) were obtained.

3. With ROH = isobutanol: **5c** (155 mg, 16%), **6c** (58 mg, 6%) and **4c** (769 mg, 78%) were obtained.

Acylation–chlorination mechanism. *1. Use of pure $SOCl_2$.* The preparation of a mixture of **4b**, **5b** and **6b** is described in the general procedure: 10 mL of pure $SOCl_2$, 600 mg (2.5 mmol) of 3,3′-bis(hydroxycarbonyl)-2,2′-bipyridine **2** and 1 mL of EtOH afforded a mixture of **5b** (46 mg, 5%), **6b** (18 mg, 2%) and the diester **4b** (702 mg, 87%).

2. Use of $SOCl_2$–Cl_2 mixture. The synthetic method used to produce Cl_2 has been adapted from the procedure described in the literature.[16] Commercial HCl was added (15 mL; *d* = 1.7) dropwise to crystalline powder of $KMnO_4$ (10 g, 63 mmol) and the temperature of the reaction mixture was increased to 35–45 °C. The mixture was then magnetically stirred for 5 h. The mixture of gases produced (Cl_2–H_2O–HCl–ClO_2) was dried by bubbling the mixture through a saturated aqueous solution of NaCl. HCl gas was then eliminated by bubbling the remaining gas mixture (Cl_2–HCl–ClO_2) through a second tube containing $CuSO_4$ powder. Pure Cl_2 was finally obtained by bubbling the (Cl_2–ClO_2) gas mixture into a third tube containing H_2SO_4. The freshly prepared Cl_2 was then progressively bubbled into a mixture containing 6 mL of thionyl chloride and 600 mg (2.5 mmol) of 3,3′-bis(hydroxycarbonyl)-2,2′-bipyridine **2**. The mixture was refluxed for 5 h and then treated as described in the general procedure. Three compounds were obtained; **5b** (398 mg, 45%), **6b** (106 mg, 12%) and **4b** (314 mg, 39 %).

*Compound **4a**.* Mp = 135–136 °C; anal. calc. (found) for $C_{14}H_{12}N_2O_4$: C, 61.76 (61.13); H, 4.42 (4.45); N, 10.29 (9.82); *m/z* 273.0 (M^+ + H, $C_{14}H_{13}N_2O_4$ requires 273.09); IR (KBr) *ν*/cm^{-1} 1720 (C=O, s), 1582 (C=C, m), 1440 (C=N, m), 1307, 1299 (C–O, m); ^{1}H NMR (250.14 MHz, $CDCl_3$) *δ* (ppm) 8.74 (dd, 2 H, H_6,H_6', $^3J_{H6–H5}$ = 4.83 Hz, $^4J_{H6–H4}$ = 1.62 Hz), 8.37 (dd, 2 H, H_4,H_4', $^3J_{H4–H5}$ = 7.94 Hz, $^4J_{H4–H6}$ = 1.62 Hz), 7.44 (dd, 2 H, H_5,H_5', $^3J_{H5–H4}$ = 7.94 Hz, $^3J_{H5–H6}$ = 4.83 Hz), 3.66 (s, 6 H, 2 CH_3).

*Compound **5a**.* Mp = 121–122 °C; anal. calc. (found) for $C_{13}H_9N_2O_3Cl_3$: C, 44.94 (44.98); H, 2.59 (2.63); N, 8.06 (7.99); *m/z* 347.0 (M^+ + H, $C_{13}H_{10}N_2O_3Cl_3$ requires 346.98); IR (KBr) *ν*/cm^{-1} 1744 (C=O, s), 1717 (C=O, s), 1601, 1581 (C=C, w), 1434 (C=N, m), 1297 (C–O, w); ^{1}H NMR (250.14 MHz; $CDCl_3$) *δ* (ppm) 8.9 (dd, 1H, H_2, $^3J_{H2–H3}$ = 4.9 Hz, $^4J_{H2–H4}$ = 1.6 Hz), 8.2 (dd, 1 H, H_4, $^3J_{H4–H3}$ = 7.8 Hz, $^4J_{H4–H2}$ = 1.6 Hz), 7.53 (dd, 1 H, H_3, $^3J_{H3–H4}$ = 7.8 Hz, $^3J_{H3–H2}$ = 4.9 Hz), 6.49 (dd, 1 H, H_7, $^3J_{H7–H8}$ = 1.33 Hz, $^4J_{H7–H9}$ = 2.1 Hz), 5.35 (t, 1 H, H_8, $^3J_{H8–H7}$ = 1.33 Hz, $^3J_{H8–H9}$ = 1.33 Hz), 5.03 (dd, 1 H, H_9, $^3J_{H9–H8}$ = 1.33 Hz, $^4J_{H7–H9}$ = 2.1 Hz), 4.0 (s, 3 H, CH_3).

*Compound **6a**. m/z* 347.0 (M^+ + H, $C_{13}H_{10}N_2O_3Cl_3$ requires 346.98); ^{1}H NMR (200.13 MHz; $CDCl_3$) *δ* (ppm) 8.86 (dd, 1 H, H_2, $^3J_{H2–H3}$ = 4.9 Hz, $^4J_{H2–H4}$ = 1.6 Hz), 8.14 (dd, 1 H, H_4, $^3J_{H4–H3}$ = 7.8 Hz, $^4J_{H4–H2}$ = 1.6 Hz), 7.48 (dd, 1 H, H_3, $^3J_{H3–H4}$ = 7.8 Hz, $^3J_{H3–H2}$ = 4.9 Hz), 6.47 (d, 1 H, H_7, $^3J_{H7–H8}$ = 3 Hz), 5.26 (d, 1 H, H_9, $^3J_{H9–H8}$ = 9.8 Hz), 4.52 (dd, 1 H, H_8, $^3J_{H8–H7}$ = 3.05 Hz, $^3J_{H8–H9}$ = 9.75 Hz), 3.96 (s, 3 H, CH_3).

*Compound **4b**.* Mp = 89–90 °C; anal. calc. (found) for $C_{16}H_{16}N_2O_4$: C, 64.01 (63.56.); H, 5.33 (5.62); N, 9.33 (9.13); *m/z* 301.10 (M^+ + H, $C_{16}H_{17}N_2O_4$ requires 301.12); IR (KBr) *ν*/cm^{-1} 1724 (C=O, s), 1578, 1565 (C=C, w), 1423 (C=N, m), 1277 (C–O, w); ^{1}H NMR (250.14 MHz; $CDCl_3$) *δ* (ppm) 8.74 (dd, 2 H, H_6,H_6', $^3J_{H6–H5}$ = 4.80 Hz, $^4J_{H6–H4}$ = 1.56 Hz), 8.36 (dd, 2 H, H_4,H_4', $^3J_{H4–H5}$ = 7.93 Hz, $^4J_{H4–H6}$ = 1.56 Hz), 7.42 (dd, 2 H, H_5,H_5', $^3J_{H5–H4}$ = 7.93 Hz, $^3J_{H5–H6}$ = 4.80 Hz), 4.08 (q, 4 H, 2 CH_2, $^3J_{CH2–CH3}$ = 7.15 Hz), 1.02 (t, 6 H, 2 CH_3, $^3J_{CH3–CH2}$ = 7.15 Hz).

*Compound **5b**.* Mp = 102–103 °C; anal. calc. (found) for $C_{14}H_{11}N_2O_3Cl_3$: C, 46.97 (47.44); H, 3.05 (3.33); N, 7.74 (7.35); *m/z* 360.9 (M^+ + H, $C_{14}H_{12}NO_3Cl_3$ requires 360.99); IR (KBr) *ν*/cm^{-1} 1750 (C=O, s), 1716 (C=O, s), 1609, 1580 (C=C, w), 1457 (C=N, m); ^{1}H NMR (300.13 MHz; $CDCl_3$) *δ* (ppm) 8.90 (dd, 1 H, H_2, $^3J_{H2–H3}$ = 4.8 Hz, $^4J_{H2–H4}$ = 1.6 Hz), 8.21 (dd, 1 H, H_4, $^3J_{H4–H3}$ = 7.8 Hz, $4J_{H4–H2}$ = 1.6 Hz), 7.53 (dd, 1 H, H_3, $^3J_{H3–H4}$ = 7.8 Hz, $^3J_{H3–H2}$ = 4.8 Hz), 6.49 (dd, 1 H, H_7, $^3J_{H7–H8}$ = 1.45 Hz, $^4J_{H7–H9}$ = 2.04 Hz), 5.35 (t, 1 H, H_8, $^3J_{H8–H7}$ = 1.42 Hz, $^3J_{H8–H9}$ = 1.45 Hz), 5.00 (dd, 1 H, H_9, $^3J_{H9–H8}$ = 1.45 Hz, $^4J_{H9–H7}$ = 2.04 Hz), 4.48 (m, 2 H, CH_2, ^3J = 7.12 Hz), 1.39 (t, 3 H, CH_3, ^3J = 7.12 Hz).

*Compound **6b**. m/z* 360.9 (M^+ + H, $C_{14}H_{12}NO_3Cl_3$ requires 360.99); ^{1}H NMR (200.13 MHz; $CDCl_3$) *δ* (ppm) 8.85 (dd, 1 H, H_2, $^3J_{H2–H3}$ = 4.8 Hz, $^4J_{H2–H4}$ = 1.6 Hz), 8.14 (dd, 1 H, H_4, $^3J_{H4–H3}$ = 7.8 Hz, $^4J_{H4–H2}$ = 1.6 Hz), 7.48 (dd, 1 H, H_3, $^3J_{H3–H4}$ = 7.8 Hz, $^3J_{H3–H2}$ = 4.8 Hz), 6.46 (d, 1 H, H_7, $^3J_{H7–H8}$ = 3.2 Hz), 5.30 (d, 1 H, H_9, $^3J_{H9–H8}$ = 9.8 Hz), 4.53 (dd, 1 H, H_8, $^3J_{H8–H7}$ = 3.2 Hz, $^3J_{H8–H9}$ = 9.8 Hz), 4.46 (m, 2 H, CH_2, ^3J = 7.12 Hz), 1.37 (t, 3 H, CH_3, ^3J = 7.12 Hz).

*Compound **4c**.* Mp = 88–89 °C; anal. calc. (found) for $C_{20}H_{24}N_2O_4$: C, 67.42 (67.55); H, 6.74 (6.82); N, 7.86 (7.87); *m/z* 357.10 (M^+ + H, $C_{20}H_{25}N_2O_4$ requires 357.18); IR (KBr) *ν*/cm^{-1} 1713 (C=O, s), 1589, 1561 (C=C, w), 1470 (C=N, m), 1289 (C–O, w); ^{1}H NMR (250.14 MHz; $CDCl_3$) *δ* (ppm) 8.74 (dd, 2 H, H_6,H_6', $^3J_{H6–H5}$ = 4.83 Hz, $^4J_{H6–H4}$ = 1.66 Hz), 8.37 (dd, 2 H, H_4,H_4', $^3J_{H4–H5}$ = 7.93 Hz, $^4J_{H4–H6}$ = 1.66 Hz), 7.44 (dd, 2 H, H_5,H_5', $^3J_{H5–H4}$ = 7.93 Hz, $^3J_{H5–H6}$ = 4.83 Hz), 3.84 (d, 2 H, CH_2, $^3J_{CH–CH2}$ = 6.6 Hz), 1.68 (m, 2 H, 2 CH), 0.76 (d, 12 H, 4 CH_3, $^3J_{CH3–CH}$ = 6.6 Hz).

Compound ***5c***. Mp = 96–97 °C; anal. calc. (found) for $C_{16}H_{15}N_2O_3Cl$: C, 49.32 (49.23); H, 3.85(3.89); N, 7.19 (6.99); *m*/*z* 388.90 (M^+ + H, $C_{16}H_{16}N_2O_3Cl_3$ requires 389.02); IR (KBr) ν/cm^{-1} 1750 (C=O, s), 1715 (C=O, s), 1582 (C=C, w), 1473 (C=N, m); ^{1}H NMR (200.131 MHz; $CDCl_3$) δ (ppm) 8.88 (dd, 1 H, H_2, $^3J_{H2–H3}$ = 4.86 Hz, $^4J_{H2–H4}$ = 1.6 Hz), 8.21 (dd, 1 H, H_4, $^3J_{H4–H3}$ = 7.8 Hz, $^4J_{H4–H2}$ = 1.6 Hz), 7.52 (dd, 1 H, H_3, $^3J_{H3–H4}$ = 7.8 Hz, $^3J_{H3–H2}$ = 4.86 Hz), 6.50 (dd, 1 H, H_7, $^3J_{H7–H8}$ = 1.39 Hz, $^4J_{H7–H9}$ = 2.04 Hz), 5.36 (t, 1 H, H_8, $^3J_{H8–H7}$ = 1.39 Hz, $^3J_{H8–H9}$ = 1.39 Hz), 5.03 (dd, 1 H, H_9, $^3J_{H9–H8}$ = 1.39 Hz, $^4J_{H9–H7}$ = 2.04 Hz), 4.22 (m, 2 H, CH_2, ^3J = 6.7 Hz), 2.09 (m, 1 H, H_{13}, ^3J = 6.7 Hz), 1.0 (d, 6 H, 2 CH_3, ^3J = 6.7 Hz).

Compound ***6c***. *m*/*z* 388.90 (M^+ + H, $C_{16}H_{16}N_2O_3Cl_3$ requires 389.02); IR (KBr) ν/cm^{-1} 1750 (C=O, s), 1715 (C=O, s), 1582 (C=C, w), 1473 (C=N, m); ^{1}H NMR (200.131 MHz; $CDCl_3$) δ (ppm) 8.90 (dd, 1 H, H_2, $^3J_{H2–H3}$ = 4.86 Hz, $^4J_{H2–H4}$ = 1.6 Hz), 8.18 (dd, 1 H, H_4, $^3J_{H4–H3}$ = 7.8 Hz, $^4J_{H4–H2}$ = 1.6 Hz), 7.52 (dd, 1 H, H_3, $^3J_{H3–H4}$ = 7.8 Hz, $^3J_{H3–H2}$ = 4.86 Hz), 6.52 (d, 1 H, H_7, $^3J_{H7–H8}$ = 3.07 Hz), 5.26 (d, 1 H, H_9, $^3J_{H9–H8}$ = 9.75 Hz), 4.56 (dd, 1 H, H_8, $^3J_{H8–H7}$ = 3.08 Hz, $^3J_{H8–H9}$ = 9.75 Hz), 4.21 (m, 2 H, CH_2, ^3J = 6.67 Hz), 2.09 (m, 1 H, CH, ^3J = 6.7 Hz), 1.04 (d, 6 H, 2 CH_3, ^3J = 6.7 Hz).

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