7-Methoxypyrrolo[1,2-*a*]quinolines *via* quinolinium N-ylides

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Abstract

The pyrrolo[1,2-*a*]quinoline derivatives **4** and **6** were obtained by 1,3-dipolar cycloaddition of the quinolinium *N*-ylides in a one-pot three-component reaction under the assistance of the solvent which acts as both reaction medium and HBr scavenger. The one-pot three-component reaction could not be extended to compounds **8a-c** which were obtained in two steps. The compounds were characterized by NMR and the cycloadduct **4e** was investigated by X-ray analysis.

Keywords: one-pot three-component reaction, 1,3-dipolar cycloaddition, quinolinium *N*-ylide, pyrrolo[1,2-*a*]quinoline

Introduction

The syntheses of pyrrolo[1,2-*a*]quinoline (Figure 1) and its derivatives were reviewed in 2003 by El-Sayed and El-Sayed.[1] After this date, new methods or the improvement of the earlier methods for preparation of pyrrolo[1,2-*a*]quinoline were described in the literature.[2] Among these methods the 1,3-dipolar cycloaddition of the quinolinium ylides in presence of suitable dipolarophiles is one of the most convenient,[3] given that the heteroaromatic *N*-ylides proved to be valuable intermediates towards various N-bridgehead heterocycles.[4] The interest in pyrrolo[1,2-*a*]quinolines is due to their potential biological activity and attractive physicochemical properties.[5] Also the skeleton of pyrrolo[1,2-*a*]quinoline is present in gephyrotoxin, a natural alkaloid which was the subject of many investigations.[6]

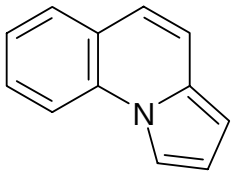


Figure 1. Pyrrolo[1,2-*a*]quinoline.

Herein is presented the synthesis of 7-methoxypyrrolo[1,2-*a*]quinolines by 1,3-dipolar cycloaddition between quinolinium *N*-ylides and acetylenic dipolarophiles. The synthetic strategy implies a one-pot three-component reaction in which the quinolinium ylide is generated *in situ* by the action of the solvent.

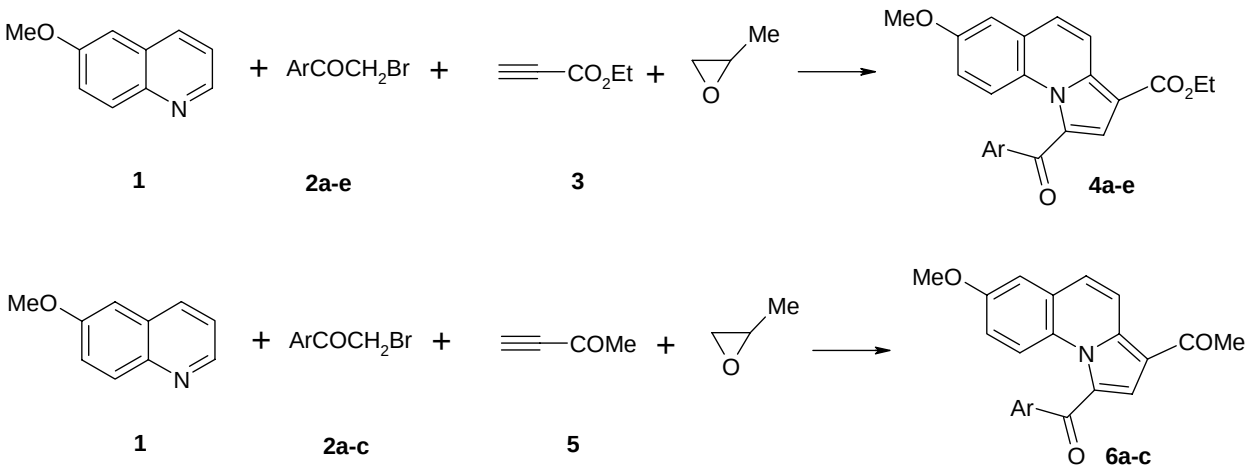
Results and Discussion

Apart from the classical multistep reactions, the multicomponent reactions which consist in converting more than two starting compounds directly to the desired products offer efficiency and good yields in obtaining various heterocycles.[7] In the classical approach towards the pyrrolo[1,2-*a*]quinolines *via* quinolinium *N*-ylides the multistep reaction consists in the previous preparation of the quinolinium salts which are converted in the next step to pyrrolo[1,2-*a*]quinolines by generating the *N*-ylide *in situ* in the presence of a base and the dipolarophile.

The materials for synthesis of 7-methoxypyrrolo[1,2-*a*]quinolines **4** were 6-methoxyquinoline **1**, substituted 2-bromoacephenones **2** and ethyl propiolate **3**. The synthesis of pyrrolo[1,2-*a*]quinolines **4** was performed in propeneoxide at room temperature. The yields of compounds **4** ranged between 50 and 60%.

Under the same reaction conditions similar results were obtained when non-symmetrical acetylenic dipolarophile ethyl propiolate is replaced by 3-butyn-2-one (Scheme 1). Thus, the new 3-acetylpyrrolo[1,2-*a*]quinoline derivatives **6a-c** were obtained in yields of 47-55%.

The reaction mechanism involves in the first step the quaternization of 6-methoxyquinoline **1** with 2-bromoacetophenones **2** to give the quinolinum bromides. Subsequently, the quinolinium *N*-ylide is generated *in situ* by the action of 1,2-epoxypropane on quinolinium bromides. Actually, the deprotonation of quinolinium bromides occurs by the action of the alkoxide ion resulted by action of bromide ion on the oxirane ring. The 1,3-dipolar cycloaddition between *N*-ylide and non-symmetrical alkynes (ethyl propiolate, 3-butyn-2-one) afforded the 7-methoxypyrrolo[1,2-*a*]quinoline **4** and **6**.

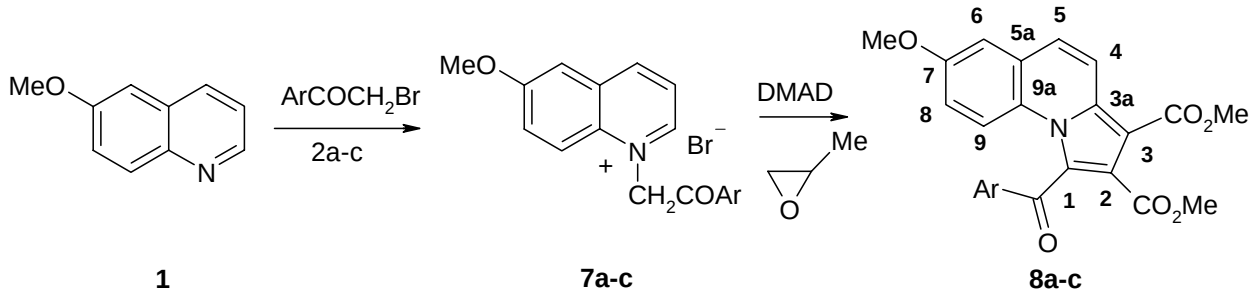


a: Ar=C_6H_5; **b**: Ar = 4-FC_6H_4; **c**: Ar=4-ClC_6H_4; **d**: Ar=4-BrC_6H_4; **e**: Ar=4-MeC_6H_4

Scheme 1

The attempts to apply the three-component method, under similar conditions, for synthesis of 7-methoxypyrrolo[1,2-a]quinolines **8** (Scheme 2) were ineffective in the case when dimethyl acetylenedicarboxylate (DMAD) was used as acetylenic dipolarophile. Probably, the reaction between quinoline and DMAD, which is more reactive than ethyl propiolate, is more favorable than the quaternization reaction between quinoline and bromoacetophenones **2**.

The compounds **8** were prepared starting with the corresponding quinolinium salts **7** obtained in a previous step by reaction of the quinolines **1** and bromoacetophenones **2a-c**. The reaction of the salts **7** with DMAD in the presence of the epoxypropane afforded the corresponding 7-methoxypyrroloquinolines (Scheme 2).



a: Ar=C_6H_5; **b**: Ar = 4-FC_6H_4; **c**: Ar=4-ClC_6H_4

Scheme 2

The compounds **4a-c** and **6a-c** were also obtained from the corresponding salts in a similar manner with compounds **8,** in comparable yields as for the one-pot three-component method.

The new pyrrolo[1,2-*a*]quinoline derivatives **4, 6** and **8** were characterized by elemental analysis, NMR spectroscopy, IR spectroscopy and by X-ray analysis for the representative compound **4e**.

In the NMR spectra the protons H-6 and H-8 of the quinoline system appear at 7.16-7.24 ppm as superimposed signals in series **4** and **6,** shielded due to their *ortho* position with respect to the methoxy group attached at C-7. However in the compounds **8** the hydrogen H-8 is more shielded than in the compounds **4** and **6** at 7.02-7.03 ppm. Due to the vicinity of the carbonyl groups attached at C-1 and C-3 the protons H-2, H-4 and H-9 are strongly deshielded. Thus in the compounds **4** and **6** the H-2 hydrogen appears as a singlet at 7.48-7.74 ppm, whereas the hydrogen H-4 appears at 8.21-8.31 ppm as a doublet with J = 9.3 Hz. The hydrogen H-9 appears as a shielded doublet at 7.97-8.09 ppm being influenced by its relative spatial position with respect to the shielding cone of the carbonyl group in the COAr moiety. In the case of compounds **8** it appears more shielded at about 7.53-7.54 ppm due to the influence of COOMe attached at C-2. The hydrogen atoms in the aliphatic and aroyl moieties present expected chemical shifts.

Table 1. Selective ^{1}H-NMR data for pyrrolo[1,2-*a*]quinolines **4**, **6** and **8**

Compd.	H-2	H-4	H-5	H-6	H-8	H-9
4	7.58-7.74	8.29-8.31	7.62-7.85	7.16-7.32	7.16-7.24	7.97-8.09
	s	d, 9.3	d, 9.3	m	m	d, 8.9
6	7.48-7.51	8.53-8.54	7.69-7.71	7.17-7.23	7.17-7.23	7.97-8.02
	s	d, 9.3	d, 9.3	m	m	d, 9.4
8	-	8.21-8.22	7.53	7.15-7.16	7.02-7.03	7.54
		d, 9.4	d, 9.4	d, 2.9	dd, 9.3, 2.9	d, 9.3

The signals in the ^{13}C-NMR spectra were solved in respect to chemical shifts and by HETCOR experiments. All the signals of the title compounds present chemical shifts different from those of the parent pyrroloquinoline[8] due to various interactions induced by substituents. The most characteristic feature is the chemical shift of carbon C-3 which appears at 107.5-107.8 ppm in compounds **4** and slightly deshielded at 115.8 ppm for series **6** due the nature of the substituent. In the compounds **8** C-3 is more shielded at around 105.4 ppm due to influence of the substituent attached at C-2. The carbon C-2 in the compounds **4** and **6** appears at about 128.8-129.4 ppm at similar chemical shift for both series. For the carbons C-9a and C-3a could be predicted that the α positions with respect to the nitrogen will induce some deshielding effect but this is partially true only for C-3a which appears at 136.5-139.9 ppm while C-9a appears shielded in the range 126.0-126.8 ppm due to its *para* position with respect to the MeO group attached at the carbon C-7. Due to their *ortho* position with respect to the MeO group, C-6 and C-8 appear shielded at 109.2-110.6 ppm and 117.9-118.4 ppm, respectively. C-7 appears at 156.9-157.0 ppm strongly deshielded by the OMe group attached to it and it is a characteristic for all the compound series.

Table 2. Selective C NMR data for pyrrolo[1,2-a]quinolines **4**, **6** and **8**

Compd.	C-6	C-3	C-8	C-4	C-9	C-2	C-5	C-7
4a-c	109.3	107.5-107.8	117.9-118.0	117.9-118.1	121.4-121.7	128.9-129.4	128.6-128.9	156.7-156.9
6a-c	109.2-109.3	115.8	118.4-118.5	118.7-118.8	121.7-121.8	128.8-129.2	129.8-130.1	157.0
8a-c	110.0-110.6	105.4	118.2-118.3	117.9-118.1	120.2-120.4	was not attributed	127.7-127.9	157.0

The IR spectra of the compounds present the characteristic absorption bands of the main functional groups. Compounds **4** and **6** present these bands at 1620-1630 cm^{-1} for the carbonyl groups in the COAr. The carbonyls in the acetyl and ethoxycarbonyl groups are observed as strong bands at around 1653-1657 cm^{-1} for the compounds **6** and 1694-1713 cm^{-1} for the compounds **4** respectively. In the compounds **8** the two carbonyl groups in the methoxycarbonyl moieties appear at about 1736 cm^{-1} and 1696 cm^{-1}. The carbonyl in the COAr moiety appears at 1639-1648 cm^{-1} very close to the values observed for compounds **4** and **6**.

Crystal data for the representative compound **4e** are reported in Table 3. The X-ray analysis confirmed the proposed structure (Figure 2, left). The presence of the 4-methylbenzoyl moiety attached to C2 gives rise to considerable molecular strain. This is due to the abnormally short non-bonded contacts observed between the atoms of the carbonyl group C16=O17 and atom C12 in ring 3 of the tricyclic system. The relevant distances are C12···O17, 2.914(2) Å and C12···C16, 3.215(2) Å, which are ~0.3 and ~0.2 Å shorter than the sums of the respective van der Waals radii.

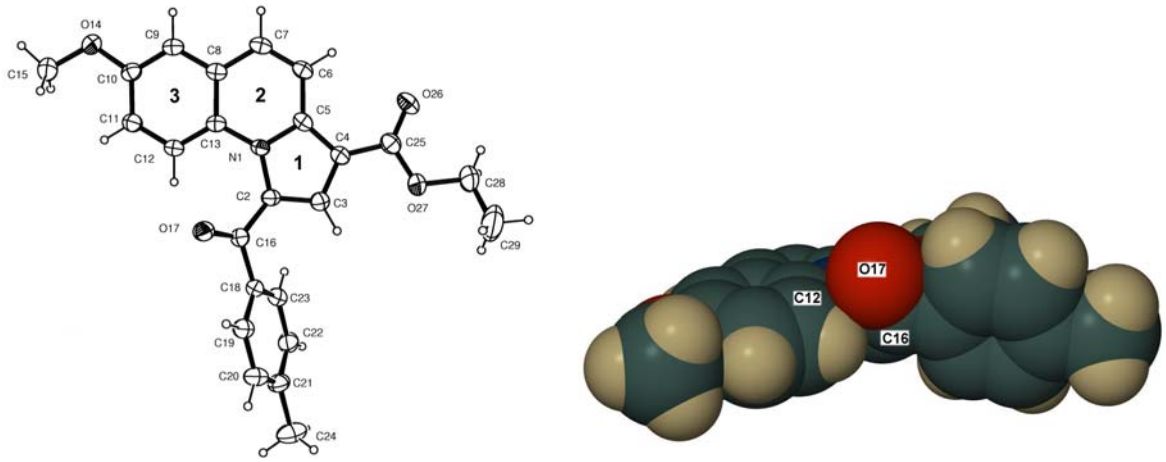


Figure 2. Left: ORTEP diagram of a molecule of **4e** with thermal ellipsoids drawn at the 50%probability level; Right: Space-filling representation showing the source of molecular distortion.

Figure 2 (right) highlights the sterically congested region, showing that atom O17 rests on the upper surface of ring 3. The repulsive interactions are balanced by the weak intramolecular hydrogen bond C12-H···O17 with H···O 2.34 Å and angle C12-H···O17 of 118°. Two consequences of this intramolecular strain are: (a) significant displacement (0.483(1) Å) of atom C16 above the plane of the five-membered ring, (b) induced helicity in the tricyclic system. The latter is reflected in the series of interplanar angles 1^2 3.7(1)°, 2^3 6.1(1)°, 1^3 9.8(1)° that indicate a convex tricyclic surface as viewed in Figure 2 (left). We recently reported analogous distortion occurring in the analogue of **4e** in which the substituent attached to C10 is a methyl group.[3h]

In the crystal of **4e**, the molecules are arranged with their tricyclic systems parallel and normal to the *b*-axis. The crystal structure is thus stabilized by several π-stacking interactions, the shortest of which are those between ring 2 of one molecule and both ring 2 (3.556(1) Å) and ring 3 (3.553(1) Å) of a 2_1-related molecule.

Table 3. Crystal data and refinement details for the representative compound **4e**[a]

Molecular formula	$C_{24}H_{21}NO_4$
M	387.42
Crystal system	Monoclinic
Space group	$P2_1/c$
a/Å	15.0758(5)
b/Å	6.5318(1)
c/Å	20.0005(7)
β/°	90.843(1)
V_{cell}/ Å^3	1969.3(1)
Z	4
T/K	173(2)
Absorption coefficient/mm^{-1}	0.089
F(000)	816
θ-range/°	1.00-26.37
Index ranges	$-18 \le h \le 18$, $-8 \le h \le 8$, $-24 \le h \le 25$
Reflections collected	4016
Observed reflections [I>2σ(I)]	2794
Data/restraints/parameters	4016/0/265
Goodness-of-fit on F^2	1.042
Final R indices [I>2σ(I)]	$R_1 = 0.0444$, $wR_2 = 0.1120$
Δρ (max., min.)/ e Å^{-3}	0.340, -0.232

[a] Full crystallographic data (CCDC 737640).

Experimental Section

General. Melting points were determined on a Boëtius hot plate microscope and are uncorrected. The elemental analysis was carried out on a COSTECH Instruments EAS32 apparatus. The IR spectra were recorded on a Nicolet Impact 410 spectrometer, in KBr pellets. The NMR spectra were recorded on a Varian Gemini 300 BB instrument, operating at 300 MHz for ^{1}H-NMR and 75 MHz for ^{13}C-NMR. Supplementary evidence was given by HETCOR and COSY experiments.

General procedure for synthesis of pyrrolo[1,2-*a*]quinolines 4 and 6

5 Mmol of 6-methoxyquinoline **1**, 5 mmol of phenacyl bromide **2** and 7 mmol of ethyl propiolate or 3-butyn-2-one in 40 mL propyleneoxide were stirred at room temperature for 40 hours. The solvent was partly removed by evaporation, 10 mL of methanol was then added and the mixture was left overnight at room temperature. The solid was filtered, washed with a MeOH-Et_2O 1:1 mixture and recrystallised from $CHCl_3$-MeOH.

Ethyl 1-benzoyl-7-methoxypyrrolo[1,2-*a*]quinoline-3-carboxylate (4a). Yellow crystals with mp 151-3 ºC were obtained by recrystallization from a methanol-$CHCl_3$ mixture; Yield 60 %. Anal. Calcd. $C_{23}H_{19}NO_4$: C 73.98; H 5.13; N 3.75. Found: C 74.22; H 5.41; N 4.03. FT-IR (cm^{-1}): 1228, 1630, 1699, 2985; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.38 (t, 3H, *J* = 7.1 Hz, $MeCH_2$); 3.91 (s, 3H, 7-MeO); 4.36 (q, 2H, *J* = 7.1 Hz, CH_2); 7.16-7.20 (m, 2H, H-6, H-8); 7.55-7.65 (m, 4H, H-5, H-3', H-4', H-5'); 7.61 (s, 1H, H-2); 8.02 (d, 1H, *J* = 8.9 Hz, H-9); 8.09 (d, 2H, *J* = 8.8 Hz, H-2', H-6'); 8.29 (d, 1H, *J* = 9.3 Hz, H-4). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 14.5 (MeCH2); 55.6 (7-OMe); 60.1 (CH2O); 107.5 (C-3); 109.3 (C-6); 117.9 (C-8); 118.1 (C-4); 121.7 (C-9); 126.3, 127.8, 127.9, 139.6 (C-1, C-3a, C-5a, C-9a,); 128.4 (C-3', C-5'); 128.6 (C-5); 129.3 (C-2); 130.1 (C-2', C-6'); 132.9 (C-4'); 138.6 (C-1'); 156.8 (C-7); 164.1 (COO); 184.8 (COAr).

Ethyl 1-(4-fluorobenzoyl)-7-methoxypyrrolo[1,2-*a*]quinoline-3-carboxylate (4b). Yellow crystals with mp 187-8ºC were obtained by recrystallization from a methanol-$CHCl_3$ mixture; Yield 58 %. Anal. Calc. $C_{23}H_{18}FNO_4$: C 70.58; H 4.64; N 3.58. Found: C 70.71; H 4.89; N 3.82. FT-IR (cm^{-1}): 1233, 1634, 1694, 2971; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.39 (t, 3H, *J* = 7.1 Hz, $MeCH_2$); 3.92 (s, 3H, 7-MeO); 4.37 (q, 2H, *J* = 7.1 Hz, CH_2); 7.16-7.24 (m, 4H, H-6, H-8, H-3', H-5'); 7.58 (s, 1H, H-2); 7.62 (d, 1H, J = 9.3 Hz, H-5); 7.98 (d, 1H, *J* = 8.9 Hz, H-9); 8.12 (dd, 2H, *J* = 8.8, 5.4 Hz, H-2', H-6'); 8.31 (d, 1H, *J* = 9.3 Hz, H-4). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 14.4 ($MeCH_2$); 55.5 (7-OMe); 60.0 (CH_2O); 107.5 (C-3); 109.3 (C-6); 117.9 (C-4, C-8); 115.7 (d, *J* = 21.9 Hz, C-3', C-5'); 121.4 (C-9); 126.2, 127.2, 127.7, 139.5 (C-1, C-3a, C-5a, C-9a); 128.7 (C-5); 128.9 (C-2); 132.4 (d, *J* = 9.0 Hz, C-2', C-6'); 134.6 (d, *J* = 3.0 Hz, C-1'); 156.7 (C-7); 163.8 (COO); 165.5 (d, *J* = 250.5 Hz, C-4'); 183.2 (COAr).

Ethyl 1-(4-chlorobenzoyl)-7-methoxypyrrolo[1,2-*a*]quinoline-3-carboxylate (4c). Yellow crystals with mp 195-6ºC were obtained by recrystallization from a methanol-$CHCl_3$ mixture; Yield 52 %. Anal. Calc. $C_{23}H_{18}ClNO_4$: C 67.73; H 4.45; Cl 8.69; N 3.43. Found: C 67.81; H 4.64; Cl 8.44; N 3.57. FT-IR (cm^{-1}): 1227, 1630, 1708, 2982; ^{1}H-NMR (300 MHz, $CDCl_3$) δ:

1.39 (t, 3H, *J* = 7.1 Hz, $MeCH_2$); 3.91 (s, 3H, 7-MeO); 4.37 (q, 2H, *J* = 7.1 Hz, CH_2); 7.16-7.20 (m, 2H, H-6, H-8); 7.53 (d, 2H, *J* = 8.8 Hz, H-3', H-5'); 7.58 (s, 1H, H-2); 7.62 (d, 1H, *J* = 9.3 Hz, H-5); 7.97 (d, 1H, *J* = 8.9 Hz, H-9); 8.02 (d, 2H, *J* = 8.8 Hz, H-2', H-6'); 8.30 (d, 1H, *J* = 9.3 Hz, H-4). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 14.6 ($MeCH_2$); 55.7 (7-OMe); 60.2 (CH_2O); 107.8 (C-3); 109.3 (C-6); 118.0 (C-4, C-8); 121.5 (C-9); 126.5, 127.4, 127.9, 139.8 (C-1, C-3a, C-5a, C-9a); 128.8 (C-3', C-5'); 128.9 (C-5); 129.4 (C-2); 131.5 (C-2', C-6'); 137.0 (C-4'); 139.2 (C-1'); 156.9 (C-7); 164.0 (COO); 183.4 (COAr).

Ethyl 1-(4-bromobenzoyl)-7-methoxypyrrolo[1,2-*a*]quinoline-3-carboxylate (4d). Yellow crystals with mp 201-2 ºC were obtained by recrystallization from a methanol-$CHCl_3$ mixture; Yield 50 %. Anal. Calc. $C_{23}H_{18}BrNO_4$: C 61.08; H 4.01; Br 17.67; N 3.10. Found: C 61.31; H 4.27; Br 17.70; N 3.42. FT-IR (cm^{-1}): 1226, 1630, 1709, 2981; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.39 (t, 3H, *J* = 7.1 Hz, $MeCH_2$); 3.92 (s, 3H, 7-MeO); 4.37 (q, 2H, *J* = 7.1 Hz, CH_2); 7.18-7.21 (m, 2H, H-6, H-8); 7.58 (s, 1H, H-2); 7.64 (d, 1H, *J* = 9.3 Hz, H-5); 7.70 (d, 2H, *J* = 8.8 Hz, H-3', H-5'); 7.95 (d, 2H, *J* = 8.8 Hz, H-2', H-6'); 8.00 (d, 1H, *J* = 8.9 Hz, H-9); 8.31 (d, 1H, *J* = 9.3 Hz, H-4). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 14.6 ($MeCH_2$); 55.6 (7-OMe); 60.2 (CH_2O); 107.8 (C-3); 109.3, 118.0 (C-6, C-8); 118.0 (C-4); 121.6 (C-9); 126.5, 127.3, 127.8, 127.9, 139.8 (C-1, C-3a, C-5a, C-9a, C-4'); 129.0 (C-5); 129.4 (C-2); 131.6, 131.8 (C-3', C-5', C-2', C-6'); 137.4 (C-1'); 157.0 (C-7); 164.0 (COO); 183.6 (COAr).

Ethyl 1-(4-methylbenzoyl)-7-methoxypyrrolo[1,2-*a*]quinoline-3-carboxylate (4e). Yellow crystals with mp 157-9 ºC were obtained by recrystallization from a methanol-chloroform mixture; Yield 50 %. Anal. Calcd. $C_{24}H_{21}NO_4$: C 77.40; H 5.46; N 3.62. Found: C 77.18; H 5.77; N 3.81. FT-IR (cm^{-1}): 1224, 1625, 1713, 2937. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.39 (t, 3H, *J* = 7.1 Hz, $MeCH_2$); 2.48 (s, 3H, MeAr); 3.90 (s, 3H, 7-MeO); 4.34 (q, 2H, *J* = 7.1 Hz, CH_2); 7.15-7.18 (m, 2H, H-6, H-8); 7.36 (d, 2H, *J* = 8.3 Hz, H-3', H-5'); 7.59 (s, 1H, H-2); 7.60 (d, 1H, *J* = 9.3 Hz, H-5); 7.97-8.01 (m, 3H, H-9, H-2', H-6'); 8.30 (d, 1H, *J* = 9.3 Hz, H-4). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 14.6 ($MeCH_2$); 21.8 (4'-Me); 55.6 (7-OMe); 60.1 (CH_2O); 107.4 (C-3); 109.3 (C-6); 117.9; 118.0 (C-4, C-8); 121.6 (C-9); 126.4, 127.8, 127.9, 139.4 (C-1, C-3a, C-5a, C-9a); 128.5 (C-5); 128.7 (C-2); 129.2 (C-3', C-5'); 130.3 (C-2', C-6'); 135.9 (C-1'); 143.7 (C-4'); 156.8 (C-7); 164.2 (COO); 184.8 (COAr).

3-Acetyl-1-benzoyl-7-methoxypyrrolo[1,2-*a*]quinoline (6a). Yellow crystals with mp 168-9 ºC were obtained by recrystallization from a methanol-$CHCl_3$ mixture; Yield 47 %. Anal. Calcd. $C_{22}H_{17}NO_3$: C 76.95; H 4.99; N 4.08. Found: C 77.26; H 5.30; N 4.19. FT-IR (cm^{-1}): 1260, 1632, 1653; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.50 (s, 3H, MeCO); 3.93 (s, 3H, 7-MeO); 7.17-7.21 (m, 2H, H-6, H-8); 7.52 (s, 1H, H-2); 7.55-7.61 (m, 2H, H-3', H-4', H-5'); 7.65-7.70 (m, 2H, H-5, H-4'); 8.02 (d, 1H, *J* = 9.4 Hz, H-9); 8.08-8.11 (m, 2H, H-2', H-6'); 8.54 (d, 1H, *J* = 9.2 Hz, H-4). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 28.2 (MeCO); 55.7 (7-OMe); 109.2 (C-6); 115.8 (C-3); 117.9 (C-8); 118.8 (C-4); 121.7 (C-9); 126.8, 127.6, 127.7, 139.0 (C-1, C-3a, C-5a, C-9a); 128.6 (C-3', C-5'); 129.2 (C-2); 129.8 (C-5); 130.1 (C-2', C-6'); 132.9 (C-4'); 138.6 (C-1'); 157.0 (C-7); 184.8 (COAr); 193.5 (COMe).

3-Acetyl-1-(4-fluorobenzoyl)-7-methoxypyrrolo[1,2-*a*]quinoline (6b). Yellow crystals with mp 209-210 ºC were obtained by recrystallization from a methanol-$CHCl_3$ mixture; Yield 51 %. Anal. Calc. $C_{22}H_{16}FNO_3$: C 73.12; H 4.46; N 3.88. Found: C 73.44; H 4.29; N 3.71. FT-IR (cm^{-1}): 1254, 1630, 1657, 2971; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.51 (s, 3H, MeCO); 3.92 (s, 3H, 7-MeO); 7.17-7.22 (m, 2H, H-6, H-8); 7.25 (t, 2H, *J* = 8.8 Hz, H-3', H-5'); 7.48 (s, 1H, H-2); 7.69 (d, 1H, *J* = 9.3 Hz, H-5); 7.97 (d, 1H, *J* = 9.4 Hz, H-9); 8.13 (dd, 2H, *J* = 8.8, 5.4 Hz, H-2', H-6'); 8.53 (d, 1H, *J* = 9.3 Hz, H-4). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 28.1 (MeCO); 55.7 (7-OMe); 109.3 (C-6); 115.7 (d, *J* = 21.9 Hz, C-3', C-5'); 115.8 (C-3); 118.4 (C-8); 118.8 (C-8); 121.7 (C-9); 126.8, 127.1, 127.5, 139.0 (C-1, C-3a, C-5a, C-9a); 128.8 (C-2); 129.8 (C-5); 132.5 (d, *J* = 9.0 Hz, C-2', C-6'); 134.9 (d, *J* = 3.0 Hz, C-1'); 157.0 (C-7); 165.7 (d, *J* = 250.5 Hz, C-4'); 183.5 (COAr); 193.3 (COMe).

3-Acetyl-1-(4-chlorobenzoyl)-7-methoxypyrrolo[1,2-*a*]quinoline (6c). Yellow crystals with mp 248-9 ºC were obtained by recrystallization from a methanol-$CHCl_3$ mixture; Yield 55 %. Anal. Calc. $C_{22}H_{16}ClNO_3$: C 69.94; H 4.27; Cl 9.38; N 3.71. Found: C 70.23; H 4.11; Cl 9.73; N 3.55. FT-IR (cm^{-1}): 1253, 1623, 1657, 2996. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.51 (s, 3H, MeCO); 3.93 (s, 3H, 7-MeO); 7.19-7.23 (m, 2H, H-6, H-8); 7.55 (d, 2H, *J* = 8.6 Hz, H-3', H-5'); 7.49 (s, 1H, H-2); 7.71 (d, 1H, *J* = 9.3 Hz, H-5); 7.98 (d, 1H, *J* = 9.3 Hz, H-9); 8.03 (d, 2H, *J* = 8.6 Hz, H-2', H-6'); 8.54 (d, 1H, *J* = 9.3 Hz, H-4). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 28.1 (MeCO); 55.7 (7-OMe); 109.3 (C-6); 115.8 (C-3); 118.5 (C-8); 118.8 (C-4); 121.7 (C-9); 126.8, 127.1, 127.5, 139.2 (C-1, C-3a, C-5a, C-9a); 128.9 (C-3', C-5'); 129.2 (C-2); 130.1 (C-5); 131.4 (C-2', C-6'); 136.9 (C-4'); 139.3 (C-1'); 157.0 (C-7); 183.5 (COAr), 193.4 (COMe).

General procedure for synthesis of 6-methoxy quinolinium bromides 7

5 Mmol of 6-methoxyquinoline **1** and 5 mmol of substituted 2-bromoacetophenone **2** in 40 mL methanol were heated at reflux temperature for 6 hours. The reaction mixture was left overnight at room temperature. The solid was filtered and washed with a MeOH-Et_2O 1:1 mixture. The bromides **7** were used without purification in the subsequent reaction.

1-(2-Phenyl-2-oxoethyl)-6-methoxyquinolinium bromide (7a). The product was recrystallized from methanol and colorless crystals with mp 199-200 ºC were obtained; Yield 95 %. Anal. Calcd. $C_{18}H_{16}BrNO_2$: C 60.35, H 4.50, Br 22.30, N 3.91. Found C 60.11, H 4.77, Br 22.58, N 4.12.

1-[2-(4-Fluorophenyl)-2-oxoethyl]-6-methoxyquinolinium bromide (7b). The product was recrystallized from ethanol and colorless crystals with mp 221-2 ºC were obtained; Yield 99 %. Anal. Calcd. $C_{18}H_{15}BrFNO_2$: N 3.72. Found N 4.01.

1-[2-(4-Chlorophenyl)-2-oxoethyl]-6-methoxyquinolinium bromide (7c). The product was recrystallized from ethanol and colorless crystals with mp 224-5 ºC were obtained; Yield 92 %. Anal. Calcd. $C_{18}H_{15}BrClNO_2$: N 3.57. Found N 3.40.

General procedure for synthesis of pyrrolo[1,2-*a*]quinolines 8a-c

5 Mmol of quaternary salt **7** and 7 mmol of DMAD in 40 mL propyleneoxide were stirred at room temperature for 24 hours. The solvent was partly removed by evaporation, 10 mL methanol was added and the mixture was left overnight at room temperature. The solid was filtered, washed on filter with a MeOH:Et_2O 1:1 mixture and recrystallised from $CHCl_3$/MeOH.

Dimethyl 1-benzoyl-7-methoxypyrrolo[1,2-*a*]quinoline-2,3-dicarboxylate (8a). Yellow crystals with mp 166-7 ºC were obtained by recrystallization from a methanol-$CHCl_3$ mixture; Yield 44 %. Anal. Calcd. $C_{24}H_{19}NO_6$: C 69.06; H 4.59; N 4.59. Found: C 69.44; H 4.39; N 4.52. FT-IR (cm^{-1}): 1253, 1639, 1709, 1730, 2956; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.42, 3.88, 3.90 (3s, 9H, 3MeO); 7.02 (dd, 1H, *J* = 9.3, 2.9 Hz, H-8); 7.16 (d, 1H, *J* = 2.9 Hz, H-6); 7.46-7.65 (m, 5H, H-5, H-9, H-3', H-4' H-5'); 7.94-7.97 (m, 2H, H-2', H-6'); 8.22 (d, 1H, *J* = 9.4 Hz, H-4). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 51.6, 52.1, 55.6 (3MeO); 105.4 (C-3); 110.0 (C-6); 117.9 (C-4); 118.2 (C-8); 120.4 (C-9); 126.0, 126.6, 127.0, 128.9, 136.5 (C-1, C-2, C-3a, C-5a, C-9a); 127.7 (C-5); 128.4 (C-3', C-5'); 129.8 (C-2', C-6'); 133.7 (C-4'); 137.8 (C-1'); 157.0 (C-7); 163.6, 165.2 (2COO); 187.7 (COAr).

Dimethyl 1-(4-fluorobenzoyl)-7-methoxypyrrolo[1,2-*a*]quinoline-2,3-dicarboxylate (8b). Yellow crystals with mp 215-6 ºC were obtained by recrystallization from a methanol-$CHCl_3$ mixture; Yield 41 %. Anal. Calcd. $C_{24}H_{18}FNO_6$: C 66.21; H 4.17; N 3.21. Found: C 66.39; H 4.50; N 3.56. FT-IR (cm^{-1}): 1262, 1648, 1701, 1724, 2953; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.49, 3.88, 3.90 (3s, 9H, 3MeO); 7.03 (dd, 1H, *J* = 9.3, 2.9 Hz, H-8); 7.15 (d, 1H, *J* = 2.9 Hz, H-6); 7.16 (t, 2H, *J* = 8.9 Hz, H-3', H-5'); 7.53 (d, 1H, *J* = 9.4 Hz, H-5); 7.54 (d, 1H, *J* = 9.3 Hz, H-9); 7.99 (dd, 2H, *J* = 8.9, 5.3 Hz, H-2', H-6'); 8.21 (d, 1H, *J* = 9.4 Hz, H-4). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 51.7, 52.4, 55.7 (3MeO); 105.4 (C-3); 110.0 (C-6); 115.9 (d, *J* = 21.9 Hz, C-3', C-5'); 118.1 (C-4); 118.3 (C-8); 120.3 (C-9); 125.6, 126.6, 127.0, 128.9, 136.5 (C-1, C-2, C-3a, C-5a, C-9a); 127.9 (C-5); 132.5 (d, *J* = 9.0 Hz, C-2', C-6'); 134.1 (d, *J* = 3.0 Hz, C-1'); 157.0 (C-7); 163.6, 165.3 (2COO); 166.2 (d, *J* = 256.4 Hz, C-4'); 186.2 (COAr).

Dimethyl 1-(4-chlorobenzoyl)-7-methoxypyrrolo[1,2-*a*]quinoline-2,3-dicarboxylate (8c). Yellow crystals with mp 192-3 ºC were obtained by recrystallization from a methanol-$CHCl_3$ mixture; Yield 42 %. Anal. Calcd. $C_{24}H_{18}ClNO_6$: C 63.79; H 4.02; Cl 7.85; N 3.10. Found: C 63.57; H 4.32; Cl 7.49; N 3.31. FT-IR (cm^{-1}): 1255, 1639, 1696, 1736, 2951; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.49, 3.89, 3.90 (3s, 9H, 3MeO); 7.03 (dd, 1H, *J* = 9.3, 2.9 Hz, H-8); 7.16 (d, 1H, *J* = 2.9 Hz, H-6); 7.46 (d, 2H, *J* = 8.8 Hz, H-3', H-5'); 7.53 (d, 1H, *J* = 9.4 Hz, H-5); 7.54 (d, 1H, *J* = 9.3 Hz, H-9); 7.90 (d, 2H, *J* = 8.8 Hz, H-2', H-6'); 8.21 (d, 1H, *J* = 9.4 Hz, H-4). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: δ: 51.7, 53.0, 55.6 (3MeO); 105.4 (C-3); 110.0 (C-6); 118.1 (C-4); 118.2 (C-8); 120.2 (C-9); 125.5, 126.6, 126.9, 128.9, 136.6 (C-1, C-2, C-3a, C-5a, C-9a); 127.9 (C-5); 129.0 (C-3', C-5'); 131.5 (C-2', C-6'); 136.1 (C-4'); 140.3 (C-1'); 157.0 (C-7); 163.5, 165.1 (2COO); 186.3 (COAr).

X-ray analysis of compound 4e

A crystal fragment of dimensions 0.30 x 0.25 x 0.21 mm was mounted on a Nonius Kappa CCD diffractometer and cooled in a stream of nitrogen vapor during intensity data-collection. Program COLLECT[9] was used to determine data-collection strategy which involved ϕ- and ω-scans of 1.00°. DENZO-SMN[10] was used for data-reduction and unit cell refinement. Lorentz-polarization corrections were applied to the intensity data and the structure was routinely solved by direct methods (SHELXS-97)[11] and refined by full-matrix least-squares against F^2 (SHELXL-97).[12] All H atoms were located in difference electron density maps but were added in idealized positions in a riding model with U_{iso} set at 1.2-1.5 times those of their parent atoms. Two alternative orientations of the methyl H atoms on C24 were evident from an advanced difference Fourier synthesis and were modeled accordingly. All non-H atoms refined anisotropically. Weights of the form $w = [\sigma^2(F_o^2) + (aP)^2 + bP]^{-1}$ with $P = [\max(F_o^2, 0) + 2F_c^2]/3$ were employed in the refinement.

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