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THE USE OF ISOQUINOLINETRIONES IN THE SYNTHESIS OF BENZO[C]PHENANTHRIDINE ALKALOIDS

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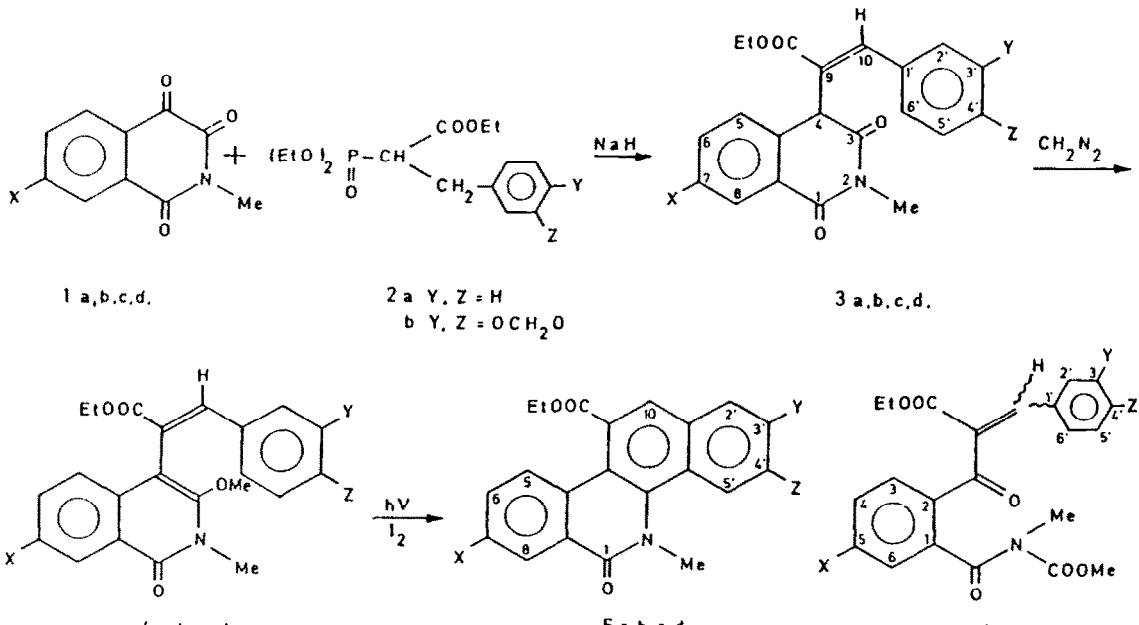
Abstract—Reaction of isoquinolinetriones **1** with phosphonates **2** yields E-ethyl α-benzylidene-1,2,3,4-tetrahydro-2-methyl-1,3-dioxo-4-isoquinolineacetates **3**. Treatment of them with diazomethane leads to the corresponding E-ethyl α-benzylidene-1,2-dihydro-3-methoxy-2-methyl-1-oxo-4-isoquinolineacetates **4**. Irradiation of the latter affords benzo[c]phenanthridones of type **5**.

Phenanthridine alkaloids have received much attention in view of their interesting pharmacologic properties; synthetic pathways towards these alkaloids—generally alkoxy substituted—have recently been reported.[1] In connection with our work[2] on alkoxy-N-alkyl-1,3,4 (2H)-isoquinolinetriones we report on their use as key intermediates in the synthesis of the benzo[c]phenanthridine skeleton. Reaction of isoquinolinetriones **1** with phosphonates **2**, yields 4-functionalized isoquinoline derivatives **3**. Methylation of **3** with diazomethane leads to the O-methylated derivatives **4** which by oxidative photocyclization can be conveniently transformed into benzo[c]phenanthridones **5** (Scheme 1).

In order to test its scope, the method has been applied to the isoquinolinetriones **1a–c** and the phosphonates **2a–b** wherein the carbalkoxy group allows functionalization. As with isatine,[3] the presence of an α-CO group allows an easy Wittig–Horner reaction on the 4-CO group. As expected, the reaction of **2b** with **1c** proceeds well at room temperature whereas heating (60°) is needed for **1b**. Instead of the primary Wittig products, the protomers **3** have been obtained. The NMR spectra show a singlet for one proton at 8.1–8.2 ppm and one at 5.2–5.4 ppm which disappears on addition of D_2O. The first singlet is ascribed to the deshielded vinyl proton, the second to the proton at C-4. The ^{13}C NMR spectrum shows two doublets at ± 144 and ± 44 ppm attributable to C-10 and C-4; three C-CO absorptions (between 160–175 ppm) are observed.

According to NMR data of the compounds **3** and of a model compound **9** obtained from the reaction of **1b** with (carbethoxyethylidene)triphenylphosphorane the *E*-



1 a,b,c,d. 2 a Y, Z = H; b Y, Z = OCH_2O. 3 a,b,c,d. 4 a,b,c,d. 5 a,b,c,d. 6 b

a X = H Y, Z = OCH_2O
b X = OMe Y, Z = H
c X = OMe Y, Z = OCH_2O
d X = NO_2 Y, Z = OCH_2O

Scheme 1.

Table 1. ^{1}H NMR data of the prepared benzo[c]phenanthridines **5** and their precursors **3** and **4**[a]

	8 a	4 a	5 a	3 b	4 b	5 b
H - 4	5.31 (s)	———	———	5.19 (s)	———	———
H - 5	7.04 (d x d)			6.94 (d)		7.66 (d)
	8 x 2 Hz			8 Hz		8 Hz
H - 6	7.48 (t x d)	7.2 - 7.6 (m)	7.5 - 7.7 (m)	7.06 (d x d)	7.0 - 7.3 (m)	7.24 (d x d)
	8 x 2 Hz			8 x 2 Hz		8 x 2 Hz
H - 7	7.37 (t x d)			———	———	———
	8 x 2 Hz					
H - 8	8.20 (d x d)	8.41 (d x d)	8.46 (d x d)	7.70 (d)	7.84 (d)	7.84 (d)
	8 x 2 Hz	8 x 2 Hz	8 x 2 Hz	2 Hz	2 Hz	2 Hz
H - 10	8.10 (s)	8.02 (s)	7.72 (s)	8.18 (s)	8.10 (s)	7.90 (s)
H - 2'		6.64 (d)	7.45 (s)			8.21 (d x d)
		2 Hz	(or 7.12)			(or 7.94)
	7.1 - 7.2 (m)					
H - 6'		6.88 (d x d)				———
		8 x 2 Hz				
H - 3'	———	———	———	7.2 - 7.7 (m)	7.0 - 7.3 (m)	
H - 4'	———	———	———			7.5 (m) 7.6
H - 5'	6.84 (d)	6.66 (d)	7.12 (s)			7.94 (d x d)
	8 Hz	8 Hz	(or 7.45)			(or 8.21)
MeN	3.45 (s)	3.64 (s)	3.94 (s)	3.44 (s)	3.63 (s)	3.96 (s)
$MeOC_3$	———	3.77 (s)	———	———	3.72 (s)	———
$MeOC_7$	———	———	———	3.86 (s)	3.91 (s)	4.01 (s)
OCH_2O	5.98 (s)	5.86 (s)	6.11 (s)	———	———	———
Me ester	1.02 (t)	1.22 (t)	1.35 (t)	1.06 (t)	1.24 (t)	1.35 (t)
CH_2 ester	3.98 (q)	4.24 (q)	4.44 (q)	4.03 (q)	4.26 (q)	4.45 (q)

a : to facilitate the comparison of the NMR data for the several compounds the same numbering of the C-atoms as in **3** has been used in the description of the compounds **4** and **5**; in naming the conventional rules will be followed.

3 c	4 c	5 c	3 d	4 d	5 d
5.25 (s)	———	———	5.44 (s)	———	———
6.93 (d)	7.24 (d)	7.60 (d)	7.28 (d)	7.38 (d)	7.81 (d)
8 Hz	8 Hz	8 Hz	8 Hz	8 Hz	8 Hz
7.04 (d x d)	7.10 (d x d)	7.16 (d x d)	8.27 (d x d)	8.21 (d x d)	8.36 (d x d)
8 x 2 Hz	8 x 2 Hz	8 x 2 Hz	8 x 2 Hz	8 x 2 Hz	8 x 2 Hz
———	———	———	———	———	———
7.69 (d)	7.84 (d)	7.85 (d)	8.92 (d)	9.16 (d)	9.26 (d)
2 Hz	2 Hz	2 Hz	2 Hz	2 Hz	2 Hz
8.07 (s)	8.02 (s)	7.63 (s)	8.15 (s)	8.06 (s)	7.82 (s)
	6.64 (d)	7.32 (s)		6.62 (d)	7.51 (s)
	2 Hz			2 Hz	
7.1 - 7.2 (m)			7.1 - 7.2 (m)		
	6.88 (d x d)	———		6.89 (d x d)	———
	8 x 2 Hz			8 x 2 Hz	
———	———	———	———	———	———
———	———	———	———	———	———
6.84 (d)	6.65 (d)	7.07 (s)	6.85 (d)	6.68 (d)	7.20 (s)
8 Hz	8 Hz		8 Hz	8 Hz	
3.43 (s)	3.64 (s)	3.90 (s)	3.49 (s)	3.66 (s)	3.97 (s)
———	3.74 (s)	———	———	3.89 (s)	———
3.86 (s)	3.94 (s)	4.00 (s)	———	———	———
6.00 (s)	5.86 (s)	6.12 (s)	6.01 (s)	5.88 (s)	6.16 (s)
1.05 (t)	1.22 (t)	1.35 (t)	1.13 (t)	1.25 (t)	1.37 (t)
3.99 (q)	4.24 (q)	4.44 (q)	4.04 (q)	4.26 (q)	4.47 (q)

configuration can be assigned. From the latter reaction the Wittig products **8** have also been isolated (Scheme 2). The values 6.43 and 5.84 ppm—calculated[4] without consideration of the influence of the isoquinolinone moiety—for the protons *cis* and *trans* to the carbethoxy group in **9**, are in good agreement with the experimental values 6.57 ± 0.05 and 6.00 ± 0.05 ppm. Considering the increment (1.35 ppm) of a geminal aryl group the values 7.78 and 7.19 ppm are calculated for the proton in the *E*- and *Z*-isomers **3**. The experimental value of 8.12 ± 0.05 ppm points to the *E*-configuration of products **3**.

It must be stressed that the yields of **3** have not been optimized; due to its acidic character the chromatographic separation of **3d** could only be realized on addition of MeCOOH to the solvent system.

The reaction of the compounds **3** with diazomethane proceeds well; in the ^{1}H NMR spectrum the absorption at δ 5.2–5.4 ppm disappears and a new absorption ascribed to the 3-OMe is observed at 3.7–3.9 ppm. The ^{13}C NMR spectrum is also in agreement with the O-methylated structure **4**; only two CO C absorptions are present between 163–168 ppm whereas the C-4 absorption appearing as a singlet is shifted from ± 44 to ± 100 ppm; a new peak (quartet) appears at ± 61 ppm (OMe).

An *E*-configuration can be assigned to the products **4** taking into account the singlet NMR absorption of the C-10 vinyl proton at 8-8.1 ppm and the arguments of other authors[5] who compared the absorption of an analogous compound to that of *Z*- and *E*-cinnamic acid derivatives. On thermolysis or photolysis of **4** no reaction takes place; however on irradiation at 350 nm of a non-degassed solution of **4**-in cyclohexane (**4a–c**) or methanol (**4d**)-in the presence of traces of I_2 a cyclized product is formed; in the NMR spectrum the absorptions of the C-3 OMe and the C-6′ proton disappear. The downfield shift of the C-5 proton and other protons can be ascribed to the formation of a planar system; all spectroscopic data (Experimental) are in agreement with structure **5**. After photocyclization re-aromatization by loss of methanol probably occurs.

On irradiation of **4b** at 350 or 300 nm the main product is not a phenanthridone but a product, the spectroscopic characteristics of which are in agreement with structure **6**. The formation of **6b** is probably due to a photo-oxidation of the C3-C4 double bond. If a degassed solution of **4b** is irradiated at 300 nm neither cyclization nor photo-oxidation products can be isolated. So we can conclude that the conversion of isoquinolinetriones to phenanthridines constitutes a short and useful way to get a good overall yield (22–35%). In contrast to the results of other authors[5] a single isomer is formed in the last step; an electron rich phenyl group seems however to be essential in this step.

EXPERIMENTAL

All m.ps are uncorrected. The UV and IR spectra have been taken on the Perkin–Elmer 124 and 257 spectrophotometers. For the NMR spectra a Jeol JNM-MH-100, a Varian XL-100 and a Bruker WP-80 spectrometer have been used; the mass spectra have been taken on a AEI-MS-12 (ionization energy 70 eV) apparatus. The photoreactions have been carried out in a RPR-208 Rayonet preparative Reactor equipped with RUL-3000 Å and RUL-3500 Å lamps. The isoquinolinetriones were synthesized according to known procedures: 2-methyl-1,3,4 (2 H)-isoquinolinetrione **1a**,[6] 7-methoxy-2-methyl-1,3,4 (2 H)-isoquinolinetrione **1b**[2] and 2-methyl-7-nitro-1,3,4 (2 H)-isoquinolinetrione **1c**.[7]

The triethyl α-benzylphosphonoacetates **2a** and **2b** were prepared with sodium hydride as a base and monoglyme as solvent instead of using potassium in xylene.[8] Triethyl α-benzylphosphonoacetate **2a**: yield 48%; b.p. 5 mm 200°; ^{1}H NMR δ ($CDCl_3$): 1.15 (3 H, t, J = 7, $COOCH_2\underline{C}H_3$), 1.37 (6 H, t, J = 7, $P(O)OCH_2\underline{C}H_3$), 2.8–3.7 (3 H, m, $\underline{C}H_2$-Ar and $\underline{C}H$-CH_2-Ar), 4.11 (4 H, q, J = 7, $P(O)\,O\underline{C}H_2$), 4.26 (2 H, q, J = 7, $COO\underline{C}H_2$), 7.30 (5 H, br.s, aryl-H).

Triethyl α-piperonylphosphonoacetate **2b**: yield 65%: b.p. 0.1 mm 190°; ^{1}H NMR δ($CDCl_3$): 1.20 (3 H, t, J = 7, $COOCH_2\underline{C}H_3$), 1.39 (6 H, t, J = 7), $P(O)OCH_2\underline{C}H_3$), 2.8–3.4 (3 H, m, $\underline{C}H_2$-Ar and $\underline{C}H$-CH_2-Ar), 4.15 (4 H, q, J = 7, $P(O)O\underline{C}H_2$), 4.22 (2 H, q, J = 7, $COO\underline{C}H_2$), 5.88 (2 H, s, OCH_2O), 6.5–6.8 (3 H, m, aryl-H); *m/z* (%): 358 (M^+, 19), 285 (22), 220 (100).

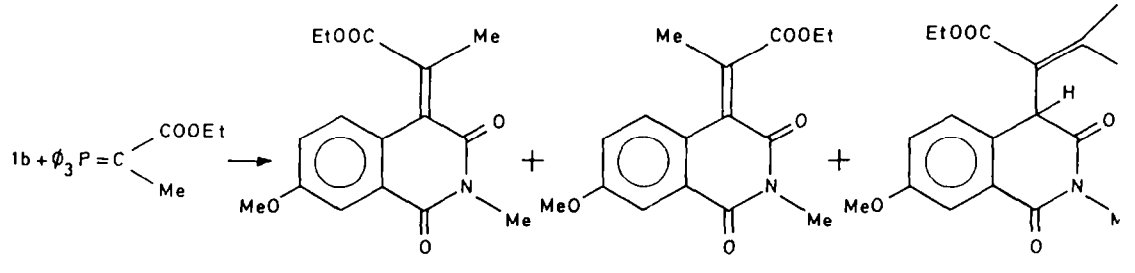
Compounds of type **3**

General method. To a suspension of NaH (0.33 mol) in 60 ml benzene, **2** (0.2 mol) dissolved in 200 ml benzene was added dropwise while keeping the temp at ± 50°. When H_2-bubbling ceased, **1** (0.1 mol), dissolved in 100 ml benzene, was added and the mixture warmed up (60°). The reaction was controlled on TLC with C_6H_6–CH_3COOEt 4:1 (solvent A) or $CHCl_3$–MeCN 15:1 (solvent B) as eluting systems. The mixture was poured into 300 ml of an ice-cold soln of NH_4Cl and extracted three times with 30 ml CH_2Cl_2. After drying and concentrating the soln, further purification of the crude product was achieved by column chromatography and crystallization from EtOH. Spectroscopic and analytical data are given below and in Tables 1 and 2.

E-Ethyl α-piperonylidene-1, 2, 3, 4-tetrahydro-2-methyl-1, 3-dioxo-4-isoquinolineacetate **3a**. Yield 46%; m.p. 158°; *m/z* (%): 393 (M^+, 52), 347 (M-EtOH, 100), 319 (347-CO, 52), 263 (M-COOEt-MeNCO, 11), 262 (319-MeNCO, 12). Exact mass calcd. for M^+ 393.1212; Found 393.1208. (Found C, 67.50; H, 5.07; N, 3.44. Calc. for $C_{22}H_{19}NO_6$: C, 67.57; H, 4.87; N, 3.56).

E-Ethyl α-benzylidene-1, 2, 3, 4-tetrahydro-7-methoxy-2-methyl-1, 3-dioxo-4-isoquinolineacetate **3b**. Yield 70%; m.p. 157°; *m/z* (%): 379 (M^+, 34), 333 (100), 305 (63), 249 (8), 248 (4). Exact mass calcd for M^+ 379.1419; Found 379.1417. (Found C, 69.69; H, 5.66; N, 3.66. Calc. for $C_{22}H_{21}NO_5$: C, 69.65; H, 5.58; N, 3.69).

E-Ethyl α-piperonylidene-1, 2, 3, 4-tetrahydro-7-methoxy-2-methyl-1, 3-dioxo-4-isoquinolineacetate **3c**. Yield 65%; m.p. 159°;



Scheme 2.

Table 2. Physical constants of the benzo[c]phenanthridines 5 and their precursors 3 and 4

	IR ($CHCl_3$) cm^{-1}					Solvent	U.V.[a] λ_{max} in nm (ε)				
	OCH_2O	OMe	COOEt	CONMe CONCO CON	NO_2						
3a	2895	—	1720	1672	—	S_1	296 sh	320(11500)			
4a	2895	2835	1704	1660	—	S_2	293(17300)	325(15800)	348 sh		
5a	2905	—	1716	1646	—	S_1	289(53200)	323(15300)	358(4500)	378(4500)	
3b	—	2835	1721	1670	—	S_1	287(8300)	310 sh	320 sh		
4b	—	2840	1710	1660	—	S_2	275(21800)	290 sh	330 sh	340(5400)	350 sh
5b	—	2840	1716	1644	—	S_1	285(32700)	325(8500)	364(6200)	377(6200)	
3c	2895	2835	1716	1670	—	S_1	322(12500)				
4c	2900	2835	1704	1660	—	S_2	286(21200)	293(21000)	325(13800)	350 sh	369 sh
5c	2905	2840	1715	1644	—	S_1	292(60200)	326(14200)	340(13100)	365 sh	381(6100)
3d	2895	—	1715	1681	1540	S_1	285(7300)	324(6500)	418(3700)	505(5400)	
4d	2900	2840	1704	1670	1520	S_1	283(11200)	296(12200)	341(22900)	368 sh	
5d	2905	—	1717	1660	1580	S_1	281(9700)	308(12600)	358(7700)	406(6600)	

a : in EtOH (S_1) or cyclohexane (S_2)

m/z (%): 423 (M^+, 29), 377 (100), 349 (61), 293 (7), 292 (4). Exact mass calcd for M^+ 423.1318; Found 423.1331. (Found C, 64.69; H, 5.10; N, 3.25. Calc for $C_{23}H_{21}NO_7$: C, 65.24; H, 5.00; N, 3.31). ^{13}C NMR δ($CDCl_3$): 13.83 ($\underline{C}H_3CH_2O$), 27.12 (CH_3N), 44.07 (C-4), 55.60 (CH_3OAr), 61.01 ($CH_3\underline{C}H_2O$), 101.69 (OCH_2O), 107.70 (C-2' or C-5'), 108.91 (C-5' or C-2'), 111.86 (C-8), 121.54 (C-6), 123.40 (C-6'), 126.46, 128.70 and 129.79 (C-4a, C-8a, C-9, C-1'), 127.50 (C-5), 143.46 (C-10), 148.49 and 148.98 (C-3' and C-4'), 159.31 (C-7), 164.84 (C-1), 165.71 (ÇOOEt), 172.05 (C-3).

E-Ethyl α-piperonylidene-1, 2, 3, 4-tetrahydro-2-methyl-7-nitro-1, 3-dioxo-4-isoquinolineacetate **3d**. Yield 53%; m.p. 161°, *m/z* (%): 438 (M^+, 50), 392 (100), 364 (50), 308 (7), 307 (4). Exact mass calc. for M^+ 438.1062; Found 438.1058. (Found, C, 60.25; H, 4.29; N, 6.29. Calc. for $C_{22}H_{18}N_2O_8$: C, 60.28; H, 4.14; N, 6.39).

Compounds of type **4**

These products have been obtained on treatment of **3a–d** with CH_2N_2 in diethyl ether as solvent. To 24 mmol **3**—dissolved in 25 ml ether—30 mmol CH_2N_2, dissolved in 180 ml ether, was added. The reaction was followed on TLC using the solvent system A or B. After evaporation of the solvent the residue was purified by column chromatography on silica gel with CCl_4-CH_3COOEt as eluent.

Spectroscopic and analytical data are given below and in Tables 1 and 2.

E-Ethyl α-piperonylidene-1, 2-dihydro-3-methoxy-2-methyl-1-oxo-4-isoquinolineacetate **4a**. Yield > 95%; m.p. 143°; *m/z* (%): 407 (*M*$^+$, 100), 346 (*M*-EtOH-Me, 8), 334 (M-COOEt, 9), 319 (334-Me, 9), 318 (346-CO, 8), 262 (319-MeNCO, 7), 261 (318-MeNCO, 23). Exact mass calcd. for M^+ 407.1369. Found 407.1364.

E-Ethyl α-benzylidene-1, 2-dihydro-3, 7-dimethoxy-2-methyl-1-oxo-4-isoquinolineacetate **4b**. Yield 63%; oil; *m/z* (%): 393 (M^+, 100), 332 (1), 320 (4), 305 (13), 304 (19), 248 (7), 247 (29). Exact mass calc. for M^+ 393.1542. Found 393.1508.

E-Ethyl α-piperonylidene-1, 2-dihydro-3, 7-dimethoxy-2-methyl-1-oxo-4-isoquinolineacetate **4c**. Yield 66%; m.p. 124°; *m/z* (%): 437 (M^+, 100), 376 (14), 364 (3), 349 (10), 348 (24), 292 (8), 291 (32). Exact mass calc. for M^+ 437.1474; Found 437.1470. (Found C, 65.60; H, 5.50; N, 311. Calc. for $C_{24}H_{23}NO_7$: C, 65.90; H, 5.30; N, 3.20). ^{13}C NMR δ ($CDCl_3$): 14.20 ($\underline{C}H_3CH_2O$), 29.00 (CH_3N), 55.60 (CH_3OAr), 61.10 ($\underline{C}H_3O$-C = C–), 61.20 ($CH_3\underline{C}H_2O$), 100.55 (C-4), 101.59 (OCH_2O), 108.59 (C-2' and C-5'), 109.16 (C-8), 122.36 (C-1'), 123.46 (C-6), 125.05 (C-4a), 125.14 (C-5), 126.97 (C-6'), 128.82 (C-9), 130.11 (C-8a), 143.47 (C-10), 148.25 (C-3' or C-4'), 148.34 (C-3), 149.39 (C-4' or C-3'), 158.38 (C-7), 162.80 (ÇOOEt), 168.32 (C-1).

E-Ethyl α-piperonylidene-1, 2-dihydro-3-methoxy-2-methyl-7-nitro-4-isoquinolineacetate **4d**. Yield > 95%; m.p. 182°; *m/z* (%): 452 (*M*$^+$, 100), 391 (10), 379 (10), 364 (12), 363 (12), 318 (7), 307 (7), 306 (27). Exact mass calc. for M^+ 452.1219; Found 452.1200.

Compounds of type **5**

An 0.1% soln in cyclohexane (**4a–c**) or MeOH (**4d**) was irradiated at 350 nm or 300 nm (**4b**) in the presence of I_2. The ppt formed during the irradiation was removed by filtration. Purification of the ppts by chromatography over silica gel using $CHCl_3$-CH_3CN mixtures afforded **5a–d**.

Reaction time, yield, spectroscopic and analytical data are given below and in the Tables 1 and 2.

Ethyl 12, 13-dihydro-12-methyl-13-oxo-[1, 3]benzodioxolo-[5, 6-c] phenanthridine-5-carboxylate **5a**. 6 Days; 79%; m.p. 208°; *m/z* (%): 375 (M^+, 100), 374 (M-H, 29), 347 (M-C_2H_4, 4), 346 (M-NMe, 12), 330 (M-OEt, 8), 302 (M-COOEt, 5). Exact mass calc. for M^+ 375.1106; Found 375.1058. (Found C, 70.28; H, 4.66; N, 3.62. Calc. for $C_{22}H_{17}NO_5$: C, 70.39; H, 4.56; N, 3.73).

Ethyl 5, 6 - dihydro - 8 - methoxy - 5 - methyl - 6 - oxo - benzo[c] phenanthridine - 11 - carboxylate **5b**. 16 Days; <5%; oil *m/z* (%): 361 (M^+, 100), 360 (23), 333 (5), 332 (11), 316 (6), 288 (5). Exact mass calc. for M^+ 361.1314; Found 361.1287.

Ethyl 12, 13-dihydro-2-methoxy-12-methyl-13-oxo-[1, 3]benzodioxolo[5, 6-c] phenanthridine-5-carboxylate **5c**. 6 Days; 64%; m.p. 193°; *m/z* (%): 405 (M^+, 100), 404 (16), 377 (4), 376 (8), 360 (7), 332 (4). Exact mass calc. for M^+ 405.1168; Found 405.1212. (Found C, 67.95; H, 4.92; N, 3.44. Calc. for $C_{23}H_{19}NO_6$: C, 68.14; H, 4.72; N, 3.45). ^{13}C NMR δ ($CDCl_3$): 14.00 ($\underline{C}H_3CH_2O$), 40.95 (CH_3N), 55.71 (CH_3OAr), 61.89 ($CH_3\underline{C}H_2O$), 101.96 (OCH_2O), 102.29 (C-5'), 105.02 (C-2'), 108.74 (C-8), 114.55 (C-6'), 121.16 (C-6), 121.81 (C-1'), 125.25 (C-10), 125.85 (C-9), 126.46 (C-8a and C-4a), 127.71 (C-5), 129.51 (C-4), 136.95 (C-3), 147.94 and 148.22 (C-3' and C-4'), 159.81 (C-7), 163.62 (ÇOOEt), 170.41 (C-1).

Ethyl 12, 13-dihydro -12 - methyl - 2 - nitro - 13 - oxo - [1, 3]benzodioxolo[5, 6-c]phenanthridine-5-carboxylate **5d**. 9 Days; 44%; m.p. 266°; *m/z* (%): 420 (M^+, 100), 419 (23), 392 (4) 391 (8), 375 (7), 373 (2), 347 (4). Exact mass calc. for M^+ 420.0957, Found 420.0935. (Found C, 62.74; H, 3.92; N, 6.55. Calc. for $C_{22}H_{16}N_2O_7$ C, 62.86; H, 3.84; N, 6.66).

Photo-oxidation product **6b**

After irradiation at 300 nm of **4b** in cyclohexane the solvent was removed and the residue purified over a silica gel column. Mixtures of $CHCl_3$ MeCN were used in this purification. A yellow oil (54%) was obtained. IR ($CHCl_3$)cm^{-1}: 2840 (OMe), 1750, 1720, 1710 and 1670 (C=O); *m/z* (%): 425 (M^+, 3), 395

(M-CH_2O, 7), 337 (M-MeNCOOMe, 27), 309 (337-CO, 7), 292 (337-OEt, 18), 264 (292-CO, 36), 263 (309-EtOH, 100). Exact mass calc. for M^+ 425.1474; Found 425.1458. ^1H NMR δ ($CDCl_3$): 1.20 (3 H, t, J = 7, $COOCH_2\underline{C}H_3$), 3.40 (3 H, s, CH_3N), 3.60 (3 H, s, CH_3OCO), 3.76 (3 H, s, CH_3OAr), 4.18 (2 H, q, $CH_3\underline{C}H_2OOC$), 6.68 (1 H, d, J_m = 2, H-6), 6.78 (1 H, d × d, J_o = 8, J_m = 2, H-4), 7.10-7.30 (5 H, m, aryl'-H), 7.60 (1 H, d, J_o = 8, H-3), 7.80 (1 H, s, vinyl H). ^{13}C NMR δ ($CDCl_3$): 14.16 ($\underline{C}H_3CH_2O$), 31.11 (CH_3N), 53.47 ($\underline{C}H_3OCO$), 55.77 ($\underline{C}H_3OAr$), 61.56 ($CH_3\underline{C}H_2O$), 112.41 (C-6 or C-4), 113.17 (C-4 or C-6), 125.69 (C-2), 128.97 (C-3'), 130.56 (C-4'), 130.83 (C-2'), 131.16 (C-1), 132.96 (C-1'), 133.67 (C-3), 142.59 (= $\underline{C}$-H), 142.80 (CO-$\underline{C}$=), 154.72 ($\underline{C}OOMe$), 164.07 (C-5), 165.22 ($\underline{C}OOCH_2CH_3$), 171.83 ($\underline{C}ON$), 193.27 ($\underline{C}O$-C=).

Preparation of model compound **9**

1 mmol **1b** and 1, 2 mmol **7** were refluxed in 5 ml benzene. Chromatography of the mixture on silica gel with CCl_4-CH_3COOEt afforded 34 mg (11%) **8**-*E*, 90 mg (30%) **8**-*Z* and 118 mg (39%) **9** with the following characteristics:

Compound **8**-E. IR ($CHCl_3$) cm^{-1}: 2835 (OMe), 1712 (COOEt), 1668 (CONCO); *m/z* (%): 303 (M^+, 26), 258 (M-OEt, 28), 257 (M-EtOH, 87), 230 (M-COOEt, 16), 229 (257-CO, 100). ^1H NMR δ ($CDCl_3$): 1.19 (3 H, *t*, $\underline{C}H_3CH_2O$), 2.47 (3 H, s, CH_3–C=), 3.39 (3 H, s, CH_3N), 3.90 (3 H, s, CH_3OAr), 4.22 (2 H, q, $CH_3\underline{C}H_2O$), 7.05 (1 H, d × d, J_o = 9, J_m = 3, H-6), 7.42 (1 H, d, J_o = 9, H-5), 7.67 (1 H, d, J_m = 3, H-8).

Compound 8-Z. IR ($CHCl_3$)cm^{-1}: 2835 (OMe), 1714 (COOEt), 1668 (CONCO); *m/z* (%): 303 (M^+, 21), 258 (27), 257 (87), 230 (16), 229 (100. ^1H NMR δ ($CDCl_3$): 1.38 (3 H, t, $\underline{C}H_3CH_2O$), 2.38 (3 H, s, CH_3-C=), 3.36 (3. H, s, CH_3N), 3.92 (3 H, s, CH_3OAr), 4.38 (2 H, q, $CH_3\underline{C}H_2O$), 7.18 (1 H, d × d, J_o = 9, J_m = 3, H-6), 7.62 (1 H, d, J_o = 9, H-5), 7.75 (1 H, d, J_m = 3, H-8).

Compound **9**. IR ($CHCl_3$)cm^{-1}: 2832 (OMe), 1716 (COOEt), 1668 (CONCO); *m/z* (%): 303 (M^+, 21), 258 (16), 257 (92), 230 (23), (229 (100). ^1H NMR δ ($CDCl_3$): 1.08 (3 H, t, $\underline{C}H_3CH_2O$), 3.38 (3 H, s, CH_3N), 3.87 (3 H, s, CH_3OAr), 4.00 (2 H, q, $CH_3\underline{C}H_2O$), 4.63 (1 H, s, H-4), 6.00 (1 H, s, H_{10}-E), 6.57 (1 H, s, H_{10}-Z), 7.12 (2 H, m, H-5 and H-6), 7.72 (1 H, d, J = 2, H-8).

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