UNPRECEDENTED REACTIVITY OF 5-SUBSTITUTED 3-HYDROXY-1,2,3,4-TETRAHYDROQUINOLINE-2,4-DIONES WITH ETHYL (TRIPHENYLPHOSPHORANYLIDENE)ACETATE

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Abstract - 3,5,8-Trisubstituted 3-hydroxy-1,2,3,4-tetrahydroquinoline-2,4-diones (**3**) reacted with ethyl (triphenylphosphoranylidene)acetate (**4**) to yield several products. The major products, 4,7-disubstituted 1,3-dihydro-3-phenylacetoxy-2*H*-indol-2-ones (**5**) and (**11**), were formed *via* the molecular rearrangement of **3**, catalyzed by the strongly basic Wittig reagent. The Wittig reaction at the lactam group of **3**, resulting in 2-ethoxycarbonylmethylene derivatives, can be explained by the poor reactivity of the sterically hindered 4-oxo group. Under acid catalysis, the Wittig reaction proceeded at the hindered 4-oxo group as well. A series of minor products were also obtained through the Wittig reaction of **3**. A reaction mechanism of the molecular rearrangement of substances (**3**) is proposed.

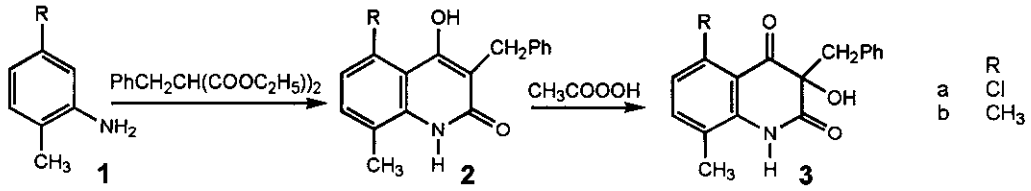
Recently, the reactions of 3-hydroxy-1,2,3,4-tetrahydroquinoline-2,4-diones, natural metabolites of some *Pseudomonas* species,[1] with ethyl (triphenylphosphoranylidene)acetate have been described.[2] These reactions proceed with high stereoselectivity to give *E*-4-ethoxycarbonylmethylene-1,2,3,4-tetrahydro-2-quinolones. 3-Substituted derivatives of 2,3*a*,4,5-tetrahydrofuro[2,3-*c*]quinoline-2,4-diones were detected and, in some cases, isolated as the minor products of the Wittig reaction. The independent synthesis of these butenolides by an intramolecular Wittig reaction has also been described.[3]

The smooth reactivity of 3-hydroxy-1,2,3,4-tetrahydroquinoline-2,4-diones in the Wittig reaction, combined with good yields, stimulated us to further our studies on a set of substrates bearing a large substituent at the position 5. These, providing the Wittig reaction occurred in the way described previously,[2] might lead to products where the newly formed exocyclic double bond would be, due to the

steric hindrance of the substituent at the position 5, out of the benzene ring plane. Besides the formation of atropisomers a change of the stereoselectivity of the Wittig reaction may be expected as well.

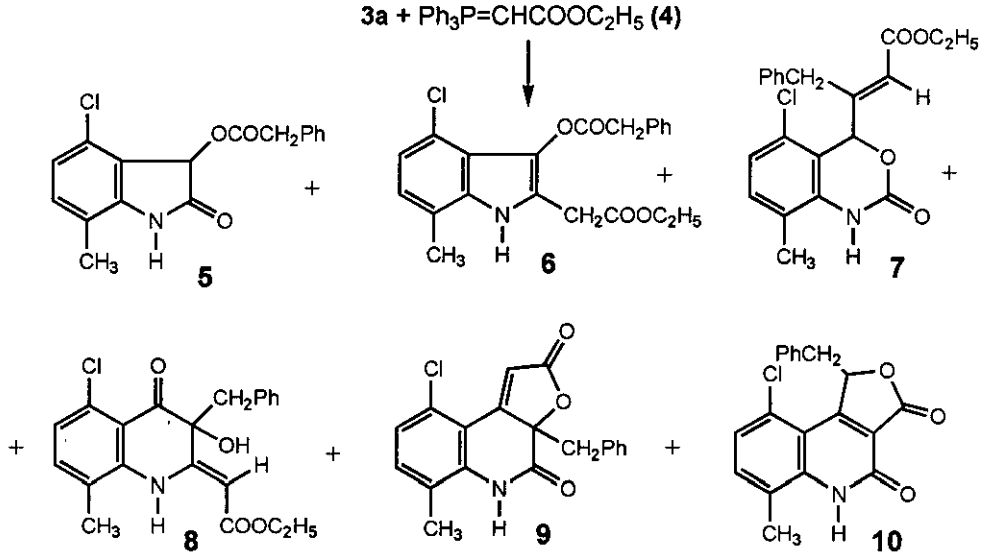
RESULTS AND DISCUSSION

Starting materials (**3a**) and (**3b**), substituted at positions 5 and 8, were prepared by the known[4] condensation of corresponding anilines (**1**) with diethyl benzylmalonate, followed by oxidation[2,5] of 4-hydroxy-2(1*H*)-quinolones (**2**) with peroxyacetic acid (Scheme 1).



Scheme 1

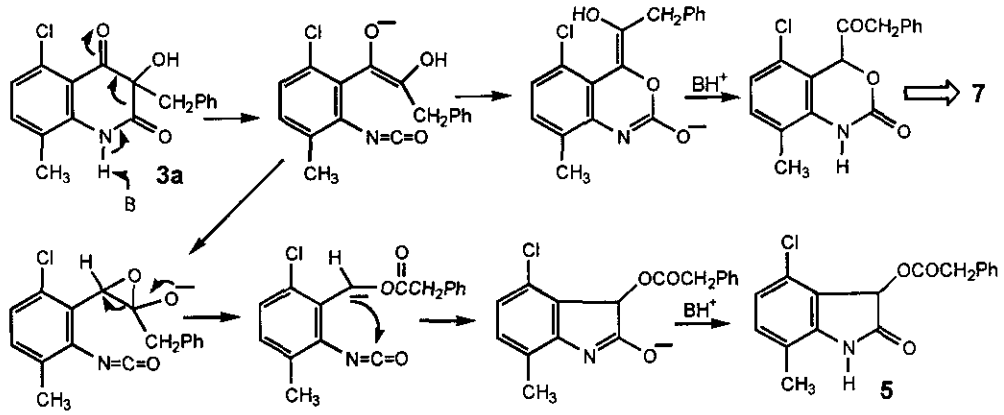
The reactions of **3a** or **3b** with ethyl (triphenylphosphoranylidene)acetate (**4**) were carried out under the same reaction conditions as in the case of unsubstituted analogues,[2] *i.e.*, by prolonged refluxing in xylene. The reaction mixtures were separated by column chromatography on silica gel.



Scheme 2

The reaction of chloro derivative (**3a**) with the Wittig reagent (**4**) resulted in the formation of six products (Scheme 2). According to the elemental composition, the main product is isomeric with **3a**. Its structure

was elucidated as indoline (**5**). Compounds (**6**, **7** and **8**) have the same empirical composition and represent the products of **3a** or its isomer with one mole of the Wittig reagent. Indole (**6**) arises from compound (**5**) *via* the Wittig reaction at the lactam group followed by the 1,3-hydrogen shift. The structure was confirmed by an independent conversion of **5** to **6** with the Wittig reagent under experimental conditions similar to those in the reaction of **3a** with **4**. Compound (**7**) was probably formed by the Wittig reaction of 4-phenylacetyl-1,4-dihydro-3,1-benzoxazin-2-one derivative The formation of the latter and also of the compound (**5**) could be explained by a base catalyzed molecular rearrangement. The suggested mechanism of the rearrangement is shown in Scheme 3, where an addition of carbanion and/or oxygen anion to the transiently formed isocyanate group is proposed. To the best of our knowledge, similar transformations of

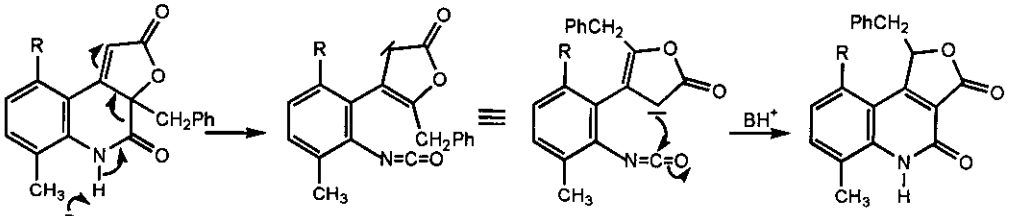


Scheme 3

amide to the isocyanate are known only for base hydrolysis of carbamic acid esters and anhydrides,[6] while the thermally reversible ring-opening ring-closure reactions *via* intermediately formed isocyanates also take place at some *N*-silylated oxazolidin-2-ones[7] and oxazolidine-2,5-diones.[8] An analogous rearrangement was not observed in the Wittig reaction of 3-hydroxy-1,2,3,4-tetrahydroquinoline-2,4-diones, unsubstituted at position 5 [2] Compound (**8**) is the product of the Wittig reaction of **3a** at the lactam group In our previous experiments[2] with tetrahydroquinoline-2,4-diones unsubstituted at position 5 an analogous reaction was not observed. Obviously, steric hindrance of the chlorine atom at C-5 prevents the Wittig reaction at the 4-oxo group.

The addition of benzoic acid to the reaction mixture is known[9] to catalyze the Wittig reaction and an enhancement of *E*-stereoselectivity was observed.[10] Therefore, we carried out the reaction of **3a** with **4** also in the presence of a 0.5 equivalent of benzoic acid and compound (**5**) was isolated as the major reaction product The second major isolated product was lactone (**9**), which was not observed when the Wittig reaction was carried out in the absence of benzoic acid. It is evident that under the catalytic effect of

benzoic acid the reaction proceeds also at the carbonyl group at position 4 However, it is not clear whether *E*-ester was formed initially (as was described in ref.[2]) and its subsequent isomerization and lactonization took place, or a change in stereoselectivity of the Wittig reaction appeared. The structure of lactone **9** was confirmed by its independent synthesis (see below). Another compound isolated in the benzoic acid catalyzed reaction was isomeric with lactone (**9**) and structure (**10**) was assigned to it as the most plausible. The migration of the benzyl group can be explained by the base catalyzed molecular rearrangement, the mechanism of which is proposed in Scheme 4.

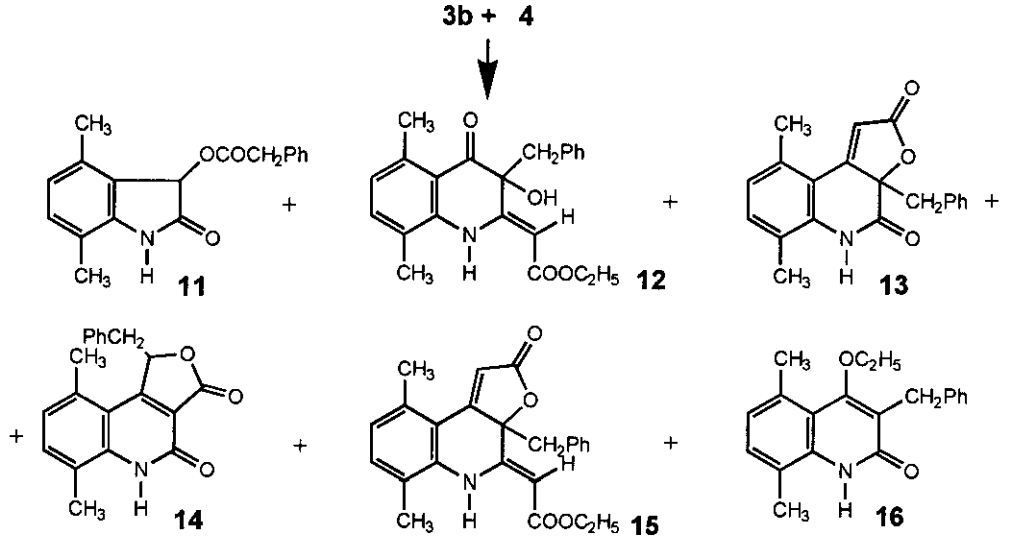


9 R = Cl
13 R = CH_3

Scheme 4

10 R = Cl
14 R = CH_3

Interestingly, only isomeric compound (**5**) was isolated in good yield, when the Wittig reaction of **3a** with **4** was carried out after conversion of the initial ylide to its acetate. It may be anticipated that the role of the acetate of ylide (**4**) is only in the basic catalysis of the molecular rearrangement and that it does not act as the Wittig reagent.

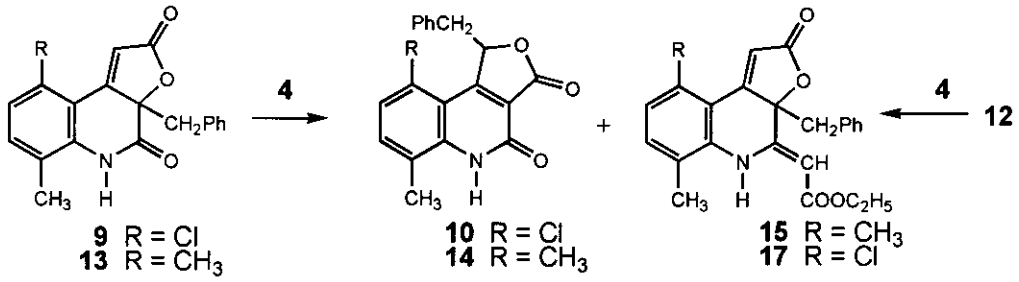


Scheme 5

In the reaction of dimethyl derivative (**3b**) with the Wittig reagent (**4**), six products were isolated (Scheme 5). Four of them (**11**, **12**, **13** and **14**) are analogous to reaction products of the reaction of **4** with **3a** and

we explain their origin as follows: indoline (**11**) is the result of the base catalyzed rearrangement of **3b** The Wittig reaction of **3a** resulted in the formation of compound (**12**) and, when the reaction was carried out under the catalytic amounts of benzoic or acetic acid, of lactone (**13**). Lactone (**14**) was formed from **13** following to the similar rearrangement as in the case of lactone (**9**) (Scheme 4).

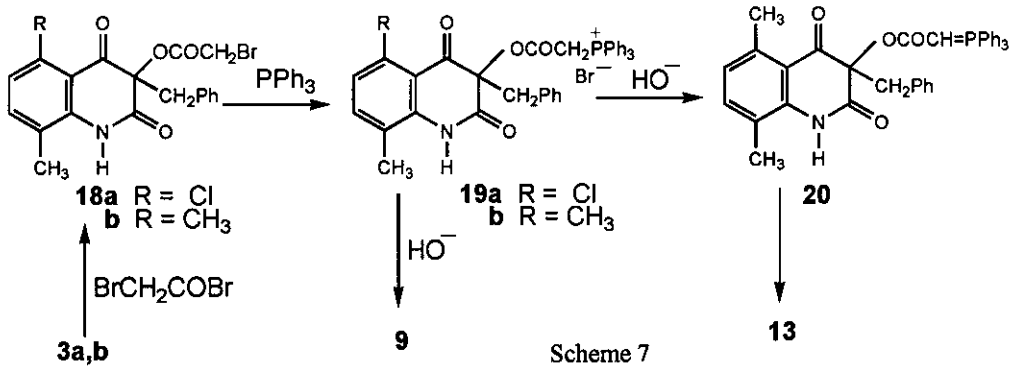
Two further isolated products (**15** and **16**) show no similarity with any of the structures of chloro derivatives (**5-10**). Compound (**15**) is the product of **3b** with two equivalents of the Wittig reagent. Its structure was confirmed by its synthesis, albeit in low yield, from ester (**12**) and the Wittig reagent (**4**) Similarly, **15** was also obtained in low yield by the reaction of lactone (**13**) with **4** The major product of the latter reaction was, however, lactone (**14**) (Scheme 6) which is most probably formed by the base catalyzed molecular rearrangement of **13** proposed in Scheme 4



Scheme 6

The structure of compound (**16**), isolated from the reaction of **3b** with **4** without the presence of catalyst, was proposed by spectral analysis and confirmed by an independent synthesis from **2b** and diethyl sulfate. In the reaction of **3b** with **4** in the presence of benzoic acid, compounds (**11**, **12**, **13** and **15**) were isolated Surprisingly, lactone (**13**) was formed together with compound (**11**) also in the reaction of **3b** with **4** in the presence of acetic acid.

The smooth reactivity of lactone (**13**) with the Wittig reagent (**4**) stimulated us to perform an analogous reaction on chloro derivative (**9**). As expected, isomerization of lactone (**9**) to lactone (**10**) took place predominantly (Scheme 6). The formation of a minor product (**17**) was found as well This compound was not isolated in the reaction of **3a** with **4** as its precursor (**9**) is not formed in the absence of an acid catalyst In order to confirm the structures of butenolides (**9**) and (**13**), their independent syntheses were carried out *via* the intramolecular Wittig reaction (Scheme 7). Initial hydroxy diones (**3a**) and (**3b**) were acylated with bromoacetyl bromide in the presence of pyridine to bromoacetyl derivatives (**18a**) and (**18b**). Their reactions with triphenylphosphane gave phosphonium salts (**19a**) and (**19b**) in good yields which in the presence of sodium hydroxide cyclized to the lactones (**9**) and (**13**).[3] The cyclization takes place *via* intermediately formed ylide, which was in the case of **20** isolated and characterized.



Scheme 7

STRUCTURE ELUCIDATION

The structure elucidation of products was performed on the basis of 1D (^{1}H and ^{13}C) and 2D (heteronuclear one-bond (HMQC) and multiple bond (HMBC) correlations) NMR experiments as well as by IR and MS spectra. In all cases the first step was the assignment of proton and carbon resonances of the benzyl group and fused benzene ring which remained unchanged during all the reaction sequences of **3a** and **3b**. Except for the essential parts, spectra will not be discussed into details. Complete spectroscopic data of compounds under investigation are given in Table I.

The indoline structure of **5** was deduced from the HMBC spectrum. The key correlations were those observed between the methine proton at δ 6.06 (H-3) bonded to carbon at δ 70.13 (C-3), and carbons resonating at δ 174.10, 121.33, 128.67 and 141.73 (C-2, C-3a, C-4 and C-7a, respectively), and simultaneously also the correlation between the NH proton and the carbon at δ 70.13 (C-3). Characteristic fragments in the mass spectrum such as *m/z* [M^+-119 ($PhCH_2CO$)+1], [M^+-135 ($PhCH_2COO$)], 91 (benzylic ion), as well as other correlations in the HMBC spectrum led to the elucidation of the structure of compound (**5**) as being a phenylacetic ester. The chemical shift of the methylene group (3.79 ppm) is also in accordance with that of the phenylacetic esters.

The comparison of ^{13}C resonances of **6** with those of **5** (especially with the resonances of the phenylacetic group), as well as occurence of the peak at *m/z* 267 (M^+-119+1) and 91 (benzylic ion) in the MS spectrum show the structural similarity of this compound with compound (**5**). Besides the correlations with neighboring carbons of the benzene ring, the NH proton exhibits an HMBC connectivity with the same two aromatic resonances at δ 121.00 and 126.74 (C-2 and C-3) as the methylene protons of the $CH_2COOC_2H_5$ group. These observations led to the presumed indole structure of **6**.

In the HMBC spectra of **7**, similar connectivities of the methine H at δ 5.92 (bonded to carbon at δ 77.56) to benzene carbons were observed, as in the spectra of compound (**5**). This could again lead to the indoline

structure, but in this case the expected correlation between NH proton and the carbon at δ 77.56 was missing. However, the only connectivity of the carbon at δ 151.26 observed was to proton at δ 5 92 in HMBC spectrum. We designated the carbon as C-2 in the 1,4-dihydro-3,1-benzoxazin-2-one structure (7), which is in agreement with data reported by Canonne *et al.*[11] The carbon at δ 77.56 and the proton at δ 5.92 were assigned to C-4 and H-4, respectively. Structure (7) was also confirmed by characteristic peaks in MS spectra at *m/z* 340 (M^+-ethoxyl+1), 312 (M^+-ethoxycarbonyl), 294 (M^+-benzyl) and 196 (5-chloro-1,4-dihydro-8-methyl-3,1-benzoxazin-2-one ring) as well as by other HMBC correlations: $PhC\underline{H}_2$/C-4, =C<u>H</u>/C-4, H-4/=<u>C</u>H, $PhC\underline{H}_2$/=<u>C</u>H, =C<u>H</u>/$PhC\underline{H}_2$, $PhC\underline{H}_2$/=C and =C<u>H</u>/=C. The *E*-configuration of the double bond was established on the basis of qualitative analysis of the NOESY spectra, where cross peaks between proton =C<u>H</u> and H-4 were observed.

The unexpected position of the newly formed C=C double bond in compound (**8**) was confirmed by an HMBC cross peak between the NH proton and the =CH carbon. Other HMBC correlations of OH and $C\underline{H}_2Ph$ protons and carbons C-2, C-3 and C-4 and of NH and =CH protons and carbon C-3 validated the structure of **8**. The *Z*-configuration of the double bond follows from the unusually low field resonance of the NH proton, which can be ascribed to an intramolecular hydrogen bond between that proton and the ester group.

Structure (**10**) was elucidated as follows: The presence of the absorption band at 1775 cm^{-1} in IR spectrum suggests a γ-lactone ring analogously to compound (**9**). The structure of this compound cannot be established from HMBC, however, in ^1H NMR spectrum, the presence of $PhCH_2CH$ fragment and the absence of the olefinic proton was observed Further contribution to the structure elucidation follows from the comparison of the ^{13}C NMR spectra of **9** and **10**. In the ^{13}C NMR spectrum of **9**, the signals of two carbonyl groups at δ 167.14 and 170.05 are present. The downfield resonating carbon corresponds to the saturated lactam group (with analogy to **3a**), the upfield to the unsaturated lactone group. In ^{13}C NMR spectrum of **10**, an upfield shift of the lactam carbonyl signal can be observed (two carbonyl signals at δ 164 71 and 165 90), which shows that the lactam ring is unsaturated and 2(1*H*)-quinolone system is present. The MS spectra of compounds (**9**) and (**10**) are very similar and, in both cases, the basic peak belongs to the benzylic ion. Similar to the comparison of ^{13}C NMR spectra of **9** and **10**, in the case of **13** and **14** it can be seen that the saturated lactame ring in **13** changes to the unsaturated ring in **14** (upfield shift of the signal at δ 170.38).

Table I. Spectroscopic Data of Compounds (**2 – 20**)

No.	MS EI, m/z (%)	IR (cm^{-1})	^1H and ^{13}C-NMR δ (ppm)
2a		3475, 3440, 3160, 1708, 1632, 1572, 1371, 1342, 1296, 1199, 820	In $CDCl_3$/DMSO-d_6: ^1H NMR: 2.42 (s, 3H, CH_3), 4.02 (s, 2H, CH_2), 7.03-7.32 (m, 7H, Ar-H), 9.81 (br s, 1H), 10.26 (br s, 1H). ^{13}C NMR: 17.57, 28.39, 112.27, 112.50, 122.61, 124.22, 125.49, 127.38, 127.85, 128.26, 130 86, 138.15, 140.19, 158.46, 162.99.
2b		3260, 3180, 1630, 1605, 1588, 1481, 1388, 1301, 1269, 1200, 1125, 1082, 818	^1H NMR (in $CDCl_3$): 2.39 (s, 3H, $C_{(8)}$-CH_3), 2.66 (s, 3H, $C_{(5)}$-CH_3), 4.12 (s, 2H, CH_2Ph), 5.89 (br s, 1H, OH), 6.86 (d, J = 7.6 Hz, 1H, H-6), 7 19 (d, J = 7.6 Hz, 1H, H-7), 7.26-7.34 (m, 5H, Ph), 8.56 (br s, 1H, NH). ^{13}C NMR (in $CDCl_3$/ /DMSO-d_6): 17.18, 24.41, 28.34, 109.55, 114.73, 120.48, 124.86, 125.55, 127.95, 128.23, 130.60, 134.43, 136.91, 140 27, 161.94, 163.59.
3a		3442, 3298, 1721, 1684, 1585, 1494, 1460, 1375, 1135, 1061, 822, 709	In $CDCl_3$: ^1H NMR : 2.28 (s, 3H, CH_3), 3.21 (s, 2H, CH_2), 3 99 (s, 1H, OH), 7.00-7.08 (m, 2H, Ph), 7.10 (d, J = 8.2 Hz, 1H, H-6), 7.15-7.23 (m, 3H, Ph), 7.26 (d, J = 8.2 Hz, 1H, H-7), 8.37 (br s, 1H, NH). ^{13}C NMR: 16.92, 46.70, 83.20, 117.21, 123.03, 126.10, 127.67, 128.14, 130.14, 132.33, 132.36, 136.70, 139.41, 170.74, 193.34.
3b		3450, 3300, 1722, 1679, 1638, 1585, 1511, 1461, 1371, 1259, 1239, 1140, 1092, 820	In $CDCl_3$: ^1H NMR: 2.29 (s, 3H, $C_{(8)}$-CH_3), 2.40 (s, 3H, $C_{(5)}$-CH_3), 3.15 and 3.25 (two d, J = 13.5 Hz, 2H, CH_2Ph), 4 03 (s, 1H, OH), 6.90 (d, J = 7.7 Hz, 1H, H-6), 7.00-7.03 (m, 2H, Ph), 7.16-7.22 (m, 3H, Ph), 7.25 (d, J = 7.7 Hz, 1H, H-7), 8.30 (s, 1H, NH). ^{13}C NMR: 16.93, 20.76, 47.02, 83.07, 118.10, 121.78, 126.62, 127.61, 128.13, 130.05, 133 19, 136 44, 138 64, 139.49, 171.32, 196.20.
5	317 (M^+, 2, ^{37}Cl), 315 (M^+, 6, ^{35}Cl), 199 (46, ^{37}Cl), 197 (100, ^{35}Cl), 182 (11, ^{37}Cl), 180 (30, ^{35}Cl), 91 (71)	3170, 3100, 2940, 1759, 1725, 1625, 1601, 1422, 1347, 1205, 1150, 822	In $CDCl_3$: ^1H NMR: 2.20 (s, 3H, $ArCH_3$), 3.79 (s, 2H, CH_2Ph), 6.06 (s, 1H, H-3), 6.89 (d, J = 8.3 Hz, 1H, H-5), 7.03 (d, J = 8.3 Hz, 1H, H-6), 7.22-7.37 (m, 5H, Ph), 8.77 (br s, 1H, NH). ^{13}C NMR: 15.81 ($Ar\underline{C}H_3$), 40.48 ($Ph\underline{C}H_2$), 70.13 (C-3), 118.50 (C-7), 121.33 (C-3a), 123.24 (C-5), 127.22 (C-4′), 128.55 (C-3′and C-5′), 128.67 (C-4), 129.39 (C-2′and C-6′), 132.76 (C-6), 133.12 (C-1′), 141.73 (C-7a), 170.15 ($PhCH_2\underline{C}O$), 174.10 (C-2).
6	387 (M^+, 3, ^{37}Cl), 385 (M^+, 9, ^{35}Cl), 269 (48, ^{37}Cl), 267 (100, ^{35}Cl), 194 (64), 91 (41)	3370, 1755, 1710, 1325, 1255, 1135, 800	In $CDCl_3$: ^1H NMR: 1.28 (t, J = 7.1 Hz, 3H, $C\underline{H}_3CH_2$), 2.37 (s, 3H, $ArCH_3$), 3 58 (s, 2H, $C_{(2)}$-CH_2), 3.95 (s, 2H, $PhCH_2$), 4.18 (q, J = 7.1 Hz, 2H, $C\underline{H}_2CH_3$), 6.82 (d, J = 7 7 Hz, 1H, H-6), 6.92 (d, J = 7.7 Hz, 1H, H-5), 7.25-7.45 (m, 5H, Ph), 8.69 (br s, 1H, NH). ^{13}C NMR: 14.10 ($\underline{C}H_3CH_2$), 15.66 ($Ar\underline{C}H_3$), 29.89 ($C_{(2)}$-$\underline{C}H_2$), 41.08 ($Ph\underline{C}H_2$), 61.62 ($\underline{C}H_2CH_3$), 117.79 (C-3a), 119.27 (C-7), 120.82 (C-5), 121.00 (C-2 or C-3), 121.22 (C-4), 123.42 (C-6), 126.74 (C-3 or C-2), 127.32 (C-4′), 128.64 (C-3′and C-5′), 129.62 (C-2′and C-6′), 133.42 (C-1′), 133.84 (C-7a), 170.04 ($\underline{C}OOC_2H_5$), 170.55 ($C_{(3)}$-$O\underline{C}O$).

Table I – continued

7	387 (M^+, 5, ^{37}Cl), 385 (M^+, 16, ^{35}Cl), 343 (16, ^{37}Cl), 341 (49, ^{35}Cl), 314 (25, ^{37}Cl), 312 (66, ^{35}Cl), 294 (26), 270 (35, ^{37}Cl), 268 (100, ^{35}Cl), 232 (38), 218 (29), 198 (15, ^{37}Cl), 196 (47, ^{35}Cl), 115 (55), 91 (58)	3250, 1712, 1650, 1592, 1490, 1460, 1388, 1308, 1174, 1035	In $CDCl_3$: ^1H NMR: 1 26 (t, J = 7.1 Hz, 3H, $C\underline{H}_3CH_2$), 2 23 (s, 3H, $ArCH_3$), 3.73 and 4.81 (two d, J = 14.3 Hz, 2 H, $PhCH_2$), 4.18 (q, J = 7.1 Hz, 2H, $C\underline{H}_2CH_3$), 5.44 (s, 1H, =CH), 5.92 (s, 1H, H-4), 6.94 (d, J = 8.2 Hz, 1H, H-6), 7.08 (d, J = 8.2 Hz, 1H, H-7), 7.17-7.34 (m, 5H, Ph), 7.73 (br s, 1H, NH). ^{13}C NMR: 14.14 ($\underline{C}H_3CH_2$), 16.22 ($Ar\underline{C}H_3$), 33.97 ($Ph\underline{C}H_2$), 60.62 ($\underline{C}H_2CH_3$), 77.56 (C-4), 115.93 (C-4a), 120.48 (=$\underline{C}$H), 121.52 (C-8), 123.69 (C-6), 126.61 (C-4′), 128.43 (C-3′and C-5′), 129.13 (C-2′and C-6′), 129.32 (C-5), 132.07 (C-7), 134.98 (C-8a), 137.12 (C-1′), 151.26 (C-2), 151.63 ($C_{(4)}\underline{C}$=), 165.80 ($\underline{C}OOC_2H_5$).
8	387 (M^+, 20, ^{37}Cl), 385 (M^+, 53, ^{35}Cl), 314 (40, ^{37}Cl), 312 (97, ^{35}Cl), 296 (44, ^{37}Cl), 294 (100, ^{35}Cl), 250 (18, ^{37}Cl), 248 (46, ^{35}Cl), 222 (11, ^{37}Cl), 220 (28, ^{35}Cl), 194 (20, ^{37}Cl), 192 (39, ^{35}Cl), 91 (76)	3460, 3230, 1700, 1670, 1630, 1580, 1460, 1285, 1245, 1150, 1045, 825, 805	In $CDCl_3$: ^1H NMR: 1.31 (t, J = 7.1 Hz, 3H, $C\underline{H}_3CH_2$), 2.34 (s, 3H, $ArCH_3$), 3.01 and 3.17 (two d, J = 13.5 Hz, 2H, CH_2Ph), 4 09 (s, 1H, OH), 4.21 (q, J = 7.1 Hz, 2H, $C\underline{H}_2CH_3$), 5.54 (s, 1H, =CH), 6.95 (d, J = 8.0 Hz, 1H, H-6), 6.98-7.04 (m, 2H, *o*-Ph), 7.18-7.27 (m, 4H, H-7, *m*-Ph and *p*-Ph), 10.64 (br s, 1H, NH). ^{13}C NMR: 14.37 ($\underline{C}H_3CH_2$), 16.86 ($ArCH_3$), 49.40 ($PhCH_2$), 59.94 ($\underline{C}H_2CH_3$), 78 48 (C-3), 89.98 (=CH), 114.87 (C-4a), 122.79 (C-8), 123.60 (C-6), 127.47 (C-4′), 128.03 (C-3′ and C-5′), 130.35 (C-2′and C-6′), 132.00 (C-5), 133.12 (C-1′), 136.49 (C-7), 142.26 (C-8a), 157.89 (C-2), 170.03 ($\underline{C}OOC_2H_5$), 193.63 (C-4).
9	341 (M^+, 3, ^{37}Cl, 339 (M^+, 9, ^{35}Cl), 250 (1, ^{37}Cl), 248 (5, ^{35}Cl), 222 (1, ^{37}Cl), 220 (3, ^{35}Cl), 166 (2, ^{37}Cl), 164 (7, ^{35}Cl), 91 (100)	3220, 1805, 1770, 1700, 1630, 1580, 1485, 1345, 1250, 1105, 1040, 930, 870	In $CDCl_3$ ^1H NMR: 2.34 (s, 3H, CH_3), 3.08 and 3.43 (two d, J = 13.7 Hz, 2H, CH_2), 6.27 (s, 1H, H-1), 6.87-7.01 (m, 2H, ArH), 7.17-7.27 (m, 5H, ArH), 8.21 (br s, 1H, NH) ^{13}C NMR: 17.18, 43.36, 86.31, 114.77, 118 50, 123.18, 125 34, 127.95, 128.32, 130 56, 130.79, 131.62, 134.46, 135.80, 157.06, 167 14, 170.05.
10	341 (M^+, 13, ^{37}Cl), 339 (M^+, 36, ^{35}Cl), 250 (21, ^{37}Cl), 248 (52, ^{35}Cl), 192 (7), 166 (7, ^{37}Cl), 164 (20, ^{35}Cl), 91 (100)	3180, 3120, 3060, 3030, 1775, 1675, 1660, 1590, 1470, 1030, 825	In DMSO-d_6: ^1H NMR: 2.47 (s, 3H, CH_3), 2.99 (dd, J_1 = 14.7 Hz, J_2 = 7.5 Hz, 1H, CH_2Ph), 3.61 (dd, J_1 = 14.7 Hz, J_3 = 2.6 Hz, 1H, CH_2Ph), 6.41 (dd, J_2 = 7.5 Hz, J_3 = 2 6 Hz, 1H, H-1), 7.09-7.15 (m, 2H, *o*-Ph), 7.20-7.31 (m, 3H, *m*-Ph and *p*-Ph), 7.42 (d, J = 7.9 Hz, 1H, H-8), 7.59 (dd, J = 7.9 Hz and 0.8 Hz, 1H, H-7), 11.51 (br s, 1H, NH). ^{13}C NMR: 17.74 ($Ar\underline{C}H_3$), 40.42 ($\underline{C}H_2Ph$), 80.17 (C-1), 112.39 (Ar), 116.39, 124.50 (Ar), 124.59 (Ar), 126.89 (C-4′), 128.23 (C-3′and C-5′), 128.27 (Ar), 129.21 (C-2′and C-6′), 135.24 (Ar), 135.64 (C-1′), 141.88 (Ar), 156.12, 164.71, 165 90
11	295 (M^+, 26), 177 (100), 160 (42), 91 (42)	3180, 3100, 1722, 1634, 1607, 1330, 1279, 1253, 1131, 1050, 801	In $CDCl_3$: ^1H NMR: 1.96 (s, 3H, $C_{(4)}$-CH_3), 2.19 (s, 3H, $C_{(7)}$-CH_3), 3.73 and 3 78 (two d, J = 14.9 Hz, 1H, CH_2Ph), 6.06 (s, 1H, H-3), 6.69 (d, J = 7.9 Hz, 1H, H-5), 6.97 (d, J = 7.9 Hz, 1H, H-6), 7.23-7.36 (m, 5H, Ph), 8.73 (br s, 1H, NH). ^{13}C NMR: 15.87 ($C_{(7)}$-$\underline{C}H_3$), 17.34

Table I – continued

			($C_{(4)}$-$\underline{C}H_3$), 40.97 (Ph$\underline{C}H_2$), 70.61 (C-3), 116.99 (C-7), 122.00 (C-3a), 124.42 (C-5), 127.31 (C-4′), 128.65 (C-3′and C-5′), 129.34 (C-2′and C-6′), 131.52 (C-6), 133.33 (C-4 and C-1′), 140.32 (C-7a), 170.22 (PhCH$_2\underline{C}$O), 174.50 (C-2).
12	365 (M^+, 55), 320 (7), 292 (81), 274 (100), 228 (56), 200 (58), 172 (31), 91 (51)	3460, 3280, 3230, 1690, 1665, 1630, 1600, 1585, 1510, 1350, 1235, 1155, 1050, 810	In $CDCl_3$: ^{1}H NMR: 1.31 (t, J = 7.2 Hz, 3H, $\underline{C}H_3CH_2$), 2.35 (s, 6H, two ArCH_3), 3.01 and 3.14 (two d, J = 13.4 Hz, 2H, CH_2Ph), 4.16 (br s, 1H, OH), 4.21 (q, J = 7.2 Hz, 2H, $C\underline{H}_2CH_3$), 5.50 (s, 1H, =CH), 6.74 (d, J = 7.3 Hz, 1H, H-6), 6.93-7.00 (m, 2H, *o*-Ph), 7.16-7.24 (m, 3H, *m*-Ph and *p*-Ph), 7.24 (d, J = 7.3 Hz, 1H, H-7), 10.53 (br s, 1H, NH). ^{13}C NMR: 14.43 ($\underline{C}H_3CH_2$), 16.84 ($C_{(8)}$-CH_3), 20.86 ($C_{(5)}$-CH_3), 49.63 ($\underline{C}H_2$Ph), 59.71 ($\underline{C}H_2CH_3$), 78.60 (C-3), 88.57 (=CH), 116.12 (C-8 or C-4a), 121.61 (C-4a or C-8), 124 21 (C-6), 127.37 (C-4′), 127.96 (C-3′and C-5′), 130.22 (C-2′and C-6′), 133.87 (C-1′), 136.41 (C-7), 139.09 (C-5), 141.38 (C-8a), 158.89 (C-2), 170.13 ($\underline{C}OOC_2H_5$), 196.34 (C-4).
13		3220, 1755, 1690, 1615, 1575, 1455, 1350, 1245, 1160, 1120, 1025, 935, 850, 820	In $CDCl_3$: ^{1}H NMR: 2.24 (s, 3H, ArCH_3), 2.33 (s, 3H, ArCH_3), 3.02 and 3.51 (two d, J = 13.7 Hz, 2H, CH_2Ph), 5.78 (s, 1H, H-1), 6.90-6.97 (m, 2H, ArH), 6.99 (d, J = 7.9 Hz, 1H, H-8), 7.18-7.28 (m, 4H, H-7 and 3x ArH), 7.83 (br s, 1H, NH). ^{13}C NMR: 17.05, 20.02, 42.85, 86.81, 115.42, 116.52, 121.75, 126.22, 127.90, 128.34, 130.29, 131.55, 133.95, 134.59, 135.86, 159.74, 167.12, 170.38.
14	319 (M^+, 55), 228 (100), 200 (6), 172 (7), 144 (19), 115 (11), 91 (60)	3190, 3060, 3020, 2980, 1775, 1670, 1655, 1595, 1570, 1470, 1350, 1210, 1030, 825, 805	In DMSO-d_6: ^{1}H NMR: 2.44 (s, 3H, ArCH_3), 2.74 (s, 3H, ArCH_3), 2.88 (dd, J_1 = 14.9 Hz, J_2 = 7.5 Hz, 1H, CH_2Ph), 3.46 (dd, J_1 = 14.9 Hz, J_3 = 2.6 Hz), 1H, CH_2Ph), 6.40 (dd, J_2 = 7.5, J_3 = 2.6 Hz, 1H, H-1, 7.07-7.15 (m, 3H, ArH and *o*-Ph), 7.18-7.30 (m, 3H, *m*-Ph and *p*-Ph), 7.48 (d, J = 7.5 Hz, 1H, ArH), 10.92 (br s, 1H, NH). ^{13}C NMR: 17.69 (ArCH_3), 21.53 (ArCH_3), 40.61 ($\underline{C}H_2$Ph), 79.91 (C-1), 113.91 (Ar), 114.58, 122.54 (Ar), 125.65 (Ar), 126.85 (C-4′), 124.16 (C-3′and C-5′), 129.21 (C-2′and C-6′), 134.12 (Ar), 134.75 (Ar), 135.50 (C-1′), 141.00 (Ar), 156.25, 166.40, 166.95.
15	389 (M^+, 100), 343 (10), 315 (43), 298 (61), 252 (40), 226 (23), 196 (24), 168 (24), 91 (52), 69 (49)	3280-3220, 3105, 2980, 1750, 1660, 1635, 1615, 1600, 1580, 1465, 1275, 1175, 1110, 940, 805	In $CDCl_3$: ^{1}H NMR: 1.32 (t, J = 7.2 Hz, 3H, $\underline{C}H_3CH_2$), 2.19 (s, 3H, $C_{(9)}$-CH_3), 2.37 (s, 3H, $C_{(6)}$-CH_3), 2.98 and 3.22 (two d, J = 13.9 Hz, CH_2Ph), 4.22 (q, J = 7.2 Hz, 2H, $C\underline{H}_2CH_3$), 5.49 (s, 1H, $C\underline{H}COOC_2H_5$), 5.69 (s, 1H, H-1), 6.84 (d, J = 7.5 Hz, H-8), 6.85-6.94 (m, 2H, *o*-Ph), 7.15-7.25 (m, 4H, H-7, *m*-Ph and *p*-Ph), 10.37 (br s, 1H, NH). ^{13}C NMR: 14.41 ($\underline{C}H_3CH_2$), 17.08 ($C_{(6)}$-CH_3), 20.12 ($C_{(9)}$-CH_3), 45.81 ($\underline{C}H_2$Ph), 59.87 ($CH_3\underline{C}H_2$), 84.57 (C-3a), 85.98 ($\underline{C}HCOOC_2H_5$), 114.08 (C-9a), 114.17 (C-1), 121.73 (C-6), 124.07 (C-8), 127.71 (C-4′), 128.25 (C-3′and C-5′), 130.32 (C-2′and C-6′), 132.43 (C-1′),

Table I - continued

			133.76 (C-7), 135.76 (C-9), 135.93 (C-5a), 154.10 (C-4),159.86 (C-9b), 170.04 ($\underline{C}OOC_2H_5$), 171.02 (C-2)
16	307 (M^+, 39), 292 (12), 278 (100), 262 (13), 202 (61), 148 (16), 131 (12), 103 (13), 91 (18), 77 (11)	3170, 3120, 3030, 2980, 2930, 1640, 1630, 1490, 1300, 1190, 1105, 1035, 815	In $CDCl_3$: ^{1}H NMR: 1.44 (t, J = 7.0 Hz, 3H, $C\underline{H}_3CH_2$), 2.38 (s, 3H, $ArCH_3$), 2.72 (s, 3H, $ArCH_3$), 3 81 (q, J = 7.0 Hz, 2H, $CH_3C\underline{H}_2$), 4.04 (s, 2H, CH_2Ph), 6.89 (d, J = 7.7 Hz, 1H, ArH), 7.10-7.18 (m, 2H, ArH and *p*-Ph), 7.20-7.27 (m, 2H, *m*-Ph), 7.33-7.40 (m, 2H, *o*-Ph), 9.30 (br s, 1H, NH). ^{13}C NMR: 15.26 ($\underline{C}H_3CH_2$), 16.98 ($ArCH_3$), 22.28 ($ArCH_3$), 30.21 (CH_2Ph), 70.49 ($CH_3\underline{C}H_2$), 116.55 (Ar), 120.59 (Ar), 122.71, 125.67 (Ar), 125.91 (C-4′), 128.26 (C-3′and C-5′), 128.53 (C-2′and C-6′), 130.82 (Ar), 133.43 (Ar), 137.00 (Ar), 140 46 (C-1′), 164.03, 164.32.
17	FAB: 410 (M^++H, 100), 391 (14), 364 (9), 336 (8), 307 (24), 289 (17), 154 (88), 136 (55), 107 (22), 91 (29)	3310, 3000, 1770, 1675, 1655, 1635, 1590, 1455, 1345, 1285, 1190, 1120, 1060, 940, 880, 820	In $CDCl_3$: ^{1}H NMR: 1.32 (t, J = 7.1 Hz, 3H, $C\underline{H}_3CH_2$), 2.36 (s, 3H, $ArCH_3$), 3.01 and 3.19 (two d, J = 13.8 Hz, 2H, $PhCH_2$), 4.22 (q, J = 7.1 Hz, 2H, $CH_3C\underline{H}_2$), 5.51 (s, 1H), 6.20 (s, 1H), 6 90-6.98 (m, 2H, ArH), 7.04 (d, J = 8.1 Hz, 1H, ArH), 7.16-7.25 (m, 4H, ArH), 10.46 (br s, 1H, NH).^{13}C NMR:14.37, 17.07, 46.20, 60 08, 83.94, 87.43, 113.07, 116.08, 122.76, 123.00, 127.74, 128.23, 130.58, 131.63, 131.73, 134.02, 137.09, 153.29, 157.00, 169.94, 170 62.
18a	437 (M^+, 3), 314 (21), 296 (53), 196 (20), 91 (100)	3230, 1760, 1720, 1690, 1580, 1490, 1460, 1360, 1290, 1130, 825	In $CDCl_3$: ^{1}H NMR: 2.13 (s, 3H, CH_3), 3.37 (s, 2H, CH_2), 4.00 and 4.05 (two d, J = 12.9 Hz, 2H, CH_2Ph), 7.00 (d, J = 8.1 Hz, 1H, ArH), 7.05-7.16 (m, 6H, ArH and Ph), 8.13 (br s, 1H, NH). ^{13}C NMR: 16.81, 24.60, 43.03, 85.33, 117.43, 122.44, 126.14, 128.03, 130.23, 130.76, 132.96, 136.53, 139.38, 165.99, 167 41, 187.68.
18b		3235, 1745, 1710, 1674, 1650, 1579, 1501, 1370, 1288, 1131, 972	In $CDCl_3$: ^{1}H NMR: 2.16 (s, 3H, $ArCH_3$), 2.48 (s, 3H, $ArCH_3$), 3.30 and 3.38 (two d, J = 13.5 Hz, 2H, CH_2Ph), 4.04 (s, 2H, CH_2Br), 6.81 (d, J = 7.7 Hz, 1 H, ArH), 7.03-7.17 (m, 6H, ArH and Ph), 8.13 (br s, 1H, NH). ^{13}C NMR: 16.78, 21.79, 24.80, 43.02, 85.63, 118.37, 121.33, 126 57, 127.87, 127.99, 130.18, 131.52, 136.36, 138.57, 140.26, 165.92, 167.74, 190.46.
19a	339 (5), 315 (3), 299 (8), 277 (100, Ph_3PO), 199 (27), 183 (24), 91 (96)	1740, 1720, 1690, 1579, 1485, 1440, 1345, 1140, 1110	In $CDCl_3$: ^{1}H NMR: 2.14 (s, 3H, CH_3), 3.12 and 3.18 (two d, J = 13.6 Hz, 2H, CH_2Ph), 5.26 (dd, J = 13.8 and 16.5 Hz, 1H, CH_2P), 5 81 (dd, J = 13.8 and 16.3 Hz, 1H, CH_2P), 6.94 (d, J = 8.1 Hz, 1H, ArH), 6.97-7.13 (m, 5H, ArH), 7.14 (d, J = 8.1 Hz, 1H, ArH), 7.61-7.71 (m, 6H, ArH), 7.71-7 81 (m, 3H, ArH), 7.81-7.94 (m, 6H, ArH), 8.36 (br s, 1H, NH). ^{13}C NMR: 17.30, 31.18, 31.93, 42.88, 86.59, 116.68, 117.10, 117.87, 123.31, 125.98, 127.89, 128.07, 130.20, 130.28, 130.38, 130.46, 132.30, 134.15, 134.30, 135.22, 135.26, 136.84, 139.36, 163.37, 163.42, 166.53, 187.01. ^{31}P NMR: 21.9 (85% H_3PO_4 external standard).
19b		3400, 1742, 1710, 1679, 1625, 1578,	In $CDCl_3$: ^{1}H NMR: 2.11 (s, 3H, $ArCH_3$), 2 33 (s, 3H, $ArCH_3$), 3.10 and 3.15 (two d, J = 13 7 Hz, 2H, CH_2Ph),

Table I - continued

	1440, 1111	5.34 (dd, J = 16.5 and 13.9 Hz, 1H, CH_2P), 5.65 (dd, J = 16.5 and 14.7 Hz, 1H, CH_2P), 6.77 (d, J = 7.8 Hz, 1H, ArH), 6.95-7.17 and 7.60-7.95 (two m, 22H, ArH, NH and four Ph). ^{31}P NMR: 21.9 (85% H_3PO_4 external standard).
20	3420, 3240, 3058, 1710, 1679, 1632, 1582, 1501, 1439, 1362, 1220, 1110	^1H NMR (in $CDCl_3$): 2.00 (s, 3H, $ArCH_3$), 2.56 (s, 3H, $ArCH_3$), 3.14 (br s, 2H, CH_2Ph), 6.65 (d, J = 7.7 Hz, 1H, ArH), 6.95-7.70 (m, 23H, ArH, =CH, NH and four Ph).

EXPERIMENTAL

Melting points were determined on a Kofler block or Gallenkamp apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 421 and 1310 spectrophotometers (KBr). NMR spectra were recorded on a Bruker DPX-300 spectrometer at 302 K in deuteriochloroform ($CDCl_3$, unless otherwise indicated) using broadband inverse-detection and $^1H/^{13}C/^{31}P/^{19}F$-QNP probehead at 300.13 MHz (^1H), 75.47 MHz (^{13}C) and 121 50 MHz (^{31}P). Chemical shifts are given on the δ scale (ppm) and are referenced to internal TMS. Some ^{13}C chemical shifts are referenced to $CDCl_3$. Heteronuclear multiple quantum coherence[12] (HMQC) experiments with BIRD presaturation were optimized for $^1J_{CH}$ of 145 Hz. Heteronuclear multiple-bond correlation[13] (HMBC) experiments were optimized for $^nJ_{CH}$ of 8 Hz. NOESY[14] spectra were measured in hexadeuteriodimethyl sulfoxide (DMSO-d_6) with mixing time of 150 and 300 ms. MS spectra were obtained on a VG-Analytical AutospecQ instrument. The spectral data of compounds under investigation are given in Table I. Column chromatography was carried out on silica gel (Kavalier, Votice) using benzene and then succesive mixtures of benzene-ethyl acetate (in ratios from 99:1 to 8:2) as eluents (solvent system S), unless otherwise indicated. The course of separation and also the purity of substances were monitored by TLC (elution systems benzene-ethyl acetate, 4:1 and chloroform-ethanol, 9:1) on Silufol UV 254 foils (Kavalier, Votice). Elemental analyses (C, H, N) were performed on a Perkin-Elmer 2400 CHN Analyzer The physical and analytical data of compounds under investigation are given in Table II

General Procedure for the Preparation of 4-Hydroxy-2(1*H*)-quinolones (2a,b). A mixture of the appropriate aniline (**1a,b**) (0.1 mol) and diethyl benzylmalonate (26.3 g, 0.105 mol) was heated on a metal bath at 200-210 °C for 1 h, at 280 °C for 1.5 h and at 295-300 °C for 45 min. Evolved ethanol was collected and weighed. After cooling, the solid product was crushed, dissolved in aqueous sodium hydroxide solution (0.5 M, 300 mL) and after filtration the solution was washed three times with toluene (50 mL). The product was precipitated from alkaline water layer with diluted (1:1) hydrochloric acid.

General Procedure for the Preparation of 3-Hydroxy-1,2,3,4-tetrahydroquinoline-2,4-diones (3a,b). To the solution of the appropriate 4-hydroxy-2(1*H*)-quinolone (**2a,b**) (20 mmol) in 0.5 M sodium hydroxide (200 mL), 20 mL (80 mmol) of 40% peroxyacetic acid in acetic acid was added dropwise under stirring at rt for 30 min. After additional stirring at rt for 30 min, the precipitated product was filtered off with suction, dispersed in 5% potassium carbonate solution (30 mL), filtered off and washed with water until the filtrate was neutral.

Reaction of 3-Benzyl-5-chloro-3-hydroxy-8-methyl-1,2,3,4-tetrahydroquinoline-2,4-dione (3a) with Ethyl (Triphenylphosphoranylidene)acetate (4). The solution of compounds (**3a**) (5.00 g, 15.8 mmol) and (**4**) (6.12 g, 17.6 mmol) in xylene (70 mL) was refluxed for 3.5 h. After cooling, the solution was evaporated to dryness *in vacuo* and the noncrystalline residue was column chromatographed on silica gel (300 g) using solvent system S. After evaporation of combined fractions and crystallization, four substances were isolated in the following elution order: yellow compound (*Z*)-3-benzyl-5-chloro-2-ethoxycarbonylmethylene-3-hydroxy-8-methyl-1,2,3,4-tetrahydroquinolin-4-one (**8**) (0.59 g, 10%), 4-chloro-2-ethoxycarbonylmethyl-7-methyl-3-phenylacetoxyindole (**6**) (0.40 g, 7%), (*E*)-4-(1-benzyl-2-ethoxycarbonylvinyl)-5-chloro-1,4-dihydro-8-methyl-3,1-benzoxazin-2-one (**7**) (0.64 g, 11%), and 4-chloro-1,3-dihydro-7-methyl-3-phenylacetoxy-2*H*-indol-2-one (**5**) (1.31 g, 26%).

Reaction of 3-Benzyl-5-chloro-3-hydroxy-8-methyl-1,2,3,4-tetrahydroquinoline-2,4-dione (3a) with Ethyl (Triphenylphosphoranylidene)acetate (4) in the Presence of Benzoic Acid. The solution of compounds (**3a**) (0.632 g, 2 mmol), (**4**) (0.730 g, 2.1 mmol), and benzoic acid (0.122 g, 1 mmol) in xylene (10 mL) was refluxed for 3 h. After cooling, the solution was washed with a sodium hydroxide solution (0.05 M, 10 mL). A separated solid interlayer was filtered off with suction to give 1-benzyl-9-chloro-6-methyl-1,3,4,5-tetrahydrofuro[3,4-*c*]quinoline-3,4-dione (**10**) (78 mg, 11%) The organic layer was dried with anhydrous sodium sulfate and, after evaporation to dryness *in vacuo,* the noncrystalline residue was column chromatographed on silica gel (30 g) using solvent system S. After evaporation of combined fractions and crystallization, three substances were isolated in the following elution order: yellow compound (**8**) (76 mg, 10%), compound (**5**) (283 mg, 45%), and 3*a*-benzyl-9-chloro-6-methyl-2,3*a*,4,5-tetrahydrofuro[2,3-*c*]quinoline-2,4-dione (**9**) (83 mg, 12%).

Reaction of 3-Benzyl-5-chloro-3-hydroxy-8-methyl-1,2,3,4-tetrahydroquinoline-2,4-dione (3a) with Ethyl (Triphenylphosphoranylidene)acetate (4) in the Presence of Acetic Acid. The solution of compounds (**3a**) (0.632 g, 2 mmol) and (**4**) (0.730 g, 2.1 mmol) in acetic acid (5 mL) was evaporated do dryness *in vacuo.* The residue was dissolved in xylene (10 mL) and refluxed for 3.5 h. After cooling, the solution was evaporated to dryness *in vacuo* and the noncrystalline residue was column chromatographed on silica gel (25 g) using solvent system S. Only one pure product (**5**) was isolated (381 mg, 60%). In the

reaction mixture, the presence of compounds (**8**) and (**3a**) was detected by TLC, the presence of lactone (**9**) was not evidenced.

Conversion of 4-Chloro-1,3-dihydro-7-methyl-3-phenylacetoxy-2*H*-indol-2-one (5) to 4-Chloro-2-ethoxycarbonylmethyl-7-methyl-3-phenylacetoxyindole (6). The solution of **5** (0.632 g, 2 mmol) and **4** (0.731 g, 2.1 mmol) in xylene (10 mL) was refluxed for 5 h. After evaporation *in vacuo* to dryness, the glassy residue was column chromatographed on silica gel (25 g) using solvent system S. Compounds (**6**) (120 mg, 16%) and (**5**) (270 mg, 43%) were obtained in pure form.

Reaction of 3*a*-Benzyl-9-chloro-6-methyl-2,3*a*,4,5-tetrahydrofuro[2,3-*c*]quinoline-2,4-dione (9) with Ethyl (Triphenylphosphoranylidene)acetate (4). The mixture of compounds (**9**) (340 mg, 1 mmol) and (**4**) (348 mg, 1 mmol) in xylene (8 mL) was refluxed for 3 h. After cooling to rt, the precipitate was filtered off with suction and 166 mg (49%) of compound (**10**) was obtained. The filtrate was evaporated to dryness *in vacuo* and column chromatographed on silica gel (25 g) using benzene as eluent. After evaporation of combined fractions and crystallization, the yellow compound (*Z*)-3*a*-benzyl-9-chloro-4-ethoxycarbonylmethylene-6-methyl-2,3*a*,4,5-tetrahydrofuro[2,3-*c*]quinolin-2-one (**17**) (171 mg, 42%) was obtained.

Reaction of 3-Benzyl-3-hydroxy-5,8-dimethyl-1,2,3,4-tetrahydroquinoline-2,4-dione (3b) with Ethyl (Triphenylphosphoranylidene)acetate (4). The solution of compounds (**3b**) (2.95 g, 10 mmol) and (**4**) (3.83 g, 11 mmol) in xylene (40 mL) was refluxed for 4 h. After cooling, the solution was evaporated to dryness *in vacuo* and washed with ether. Crystallization of the insoluble portion from benzene gave 160 mg (5%) of 1-benzyl-6,9-dimethyl-1,3,4,5-tetrahydrofuro[3,4-*c*]quinoline-3,4-dione (**14**) and, by subsequent crystallization from benzene, 0.68 g (23%) of 1,3-dihydro-4,7-dimethyl-3-phenylacetoxy-2*H*-indol-2-one (**11**). Mother liquors after the second crystallization were combined with the ether fraction and, after evaporation to dryness, column chromatographed on silica gel (85 g) using solvent system S. After evaporation of combined fractions and crystallization, four substances were isolated in the following elution order: yellow (*Z*)-3-benzyl-5,8-dimethyl-2-ethoxycarbonylmethylene-3-hydroxy-1,2,3,4-tetrahydroquinolin-4-one (**12**) (248 mg, 7%), yellow (*Z*)-3*a*-benzyl-6,9-dimethyl-4-ethoxycarbonylmethylene-2,3*a*,4,5-tetrahydrofuro[2,3-*c*]quinolin-2-one (**15**) (160 mg, 4%), 3-benzyl-5,8-dimethyl-4-ethoxy-2(1*H*)-quinolone (**16**) (667 mg, 22%) and compound **11** (160 mg, 5%, total yield 28%)

Reaction of 3-Benzyl-3-hydroxy-5,8-dimethyl-1,2,3,4-tetrahydroquinoline-2,4-dione (3b) with Ethyl (Triphenylphosphoranylidene)acetate (4) in the Presence of Benzoic Acid. The solution of **3b** (1.48 g, 5 mmol), **4** (1.91 g, 5.5 mmol), and benzoic acid (0.24 g, 2 mmol) in xylene (20 mL) was refluxed for 4 h. After cooling, the solution was washed with aqueous sodium hydrogen carbonate (5%). The organic layer was dried with anhydrous sodium sulfate and evaporated to dryness *in vacuo*. After addition of ether,

Table II. Physical and Analytical Data of Compounds (**2 – 20**)

No	Yield[15] (%)	mp (°C) (Solvent)	Formula	Analysis (%) Calcd/Found		
				C	H	N
2a	43	253-5	$C_{17}H_{14}NO_2Cl$	68.12	4.71	4.67
		(acetic acid)		68.08	4.83	4.68
2b	82	235-9	$C_{18}H_{17}NO_2$	77.40	6.13	5.01
		(acetic acid)		77.11	6.29	5.00
3a	89	192-5	$C_{17}H_{14}NO_3Cl$	64.67	4.47	4.44
		(methanol)		64.83	4.46	4 43
3b	79	175-8	$C_{18}H_{17}NO_3$	73.20	5.80	4.74
		(methanol)		73.36	6.03	4.78
5		146-8	$C_{17}H_{14}NO_3Cl$	64.67	4.47	4.44
		(benzene/*c*-C_6H_{12})		64.87	4.48	4.44
6	16	97-9	$C_{21}H_{20}NO_4Cl$	65.37	5.22	3.63
		(ether/hexane)		65.26	5.49	3.67
7		162-5	$C_{21}H_{20}NO_4Cl$	65.37	5.22	3.63
		(methanol)		65.37	5.41	3.47
8		148-54	$C_{21}H_{20}NO_4Cl$	65.37	5.22	3.63
		(methanol)		65.56	5.32	3 61
9	82	244-6	$C_{19}H_{14}NO_3Cl$	67.16	4.15	4.12
		(acetic acid)		67.20	4.19	4.02
10	49	280-4	$C_{19}H_{14}NO_3Cl$	67.16	4.15	4.12
		(acetic acid)		67.01	4.14	4.10
11		162-3	$C_{18}H_{17}NO_3$	73.20	5.80	4.74
		(methanol)		73.36	6.03	4.78
12		120-1	$C_{22}H_{23}NO_4$	72.31	6.34	3.83
		(ethyl acetate)		72.54	6.65	3 88
13	81	268-72	$C_{20}H_{17}NO_3$	75.22	5.37	4.39
		(ethanol)		75.24	5.42	4.39
14	70	282-5	$C_{20}H_{17}NO_3$	75.22	5.37	4.39
		(acetic acid)		74.81	5.48	4.46
15	20	168-71	$C_{24}H_{23}NO_4$	74.02	5.95	3.60
		(ethyl acetate)		74.09	6.30	3.57
16	59	184-8	$C_{20}H_{21}NO_2$	78.15	6.89	4 56
		(ethyl acetate)		77.90	7.09	4.53
17	42	160-2	$C_{23}H_{20}NO_4Cl$	67.40	4.92	3.42
		(hexane)		67.51	5.04	3.37
18a	81	212-14	$C_{19}H_{15}NO_4BrCl$	52.26	3.46	3.21
		(ethanol)		52.27	3.51	3.14
18b	86	176-9	$C_{20}H_{18}NO_4Br$	57.71	4.36	3.36
		(methanol)		57 98	4.33	3.38
19a	86	158-60 decomp	$C_{37}H_{30}NO_4BrClP \cdot H_2O$	61.98	4.50	1.95
				61.87	4.45	1.88
19b	73	148-50 decomp	$C_{38}H_{33}NO_4BrP$	67.26	4.90	2.06
				67.18	5.07	2.18
20	71	174-5	$C_{38}H_{32}NO_4P$	76.37	5.40	2.34
		(methanol)		75.34	5.44	2.38

a crystalline portion was obtained which, after recrystallization from methanol, gave 0.48 g (30%) of 3*a*-benzyl-6,9-dimethyl-2,3*a*,4,5-tetrahydrofuro[2,3-*c*]quinoline-2,4-dione (**13**). The ether-soluble fraction was evaporated to dryness *in vacuo* and column chromatographed on silica gel (60 g) using solvent system S. After evaporation of combined fractions and crystallization, the following substances was isolated in following elution order: yellow compound **12** (30 mg, 2%), yellow compound (**15**) (45 mg, 2%), (**3b**) (150 mg, 10%) and compound (**11**) (509 mg, 35%).

Reaction of 3-Benzyl-3-hydroxy-5,8-dimethyl-1,2,3,4-tetrahydroquinoline-2,4-dione (3b) with Ethyl (Triphenylphosphoranylidene)acetate (4) in the Presence of Acetic Acid. The solution of **3b** (1.48 g, 5 mmol) and **4** (1.92 g, 5.5 mmol) in acetic acid (5 mL) was evaporated to dryness *in vacuo*. The residue was dissolved in xylene (20 mL) and refluxed for 3 h. After cooling, the solution was evaporated to dryness *in vacuo*. After addition of ether, a crystalline portion was obtained and recrystallized from methanol to give 0.23 g (14%) of lactone (**13**). The ether-soluble fraction was evaporated to dryness *in vacuo* and column chromatographed on silica gel (90 g) using solvent system S. Compounds (**11**) (277 mg, 19%) and (**3b**) (283 mg, 19%) were isolated. The presence of compounds (**13**) and (**3b**) was detected in the reaction mixture by TLC.

Reaction of (*Z*)-3-Benzyl-5,8-dimethyl-2-ethoxycarbonylmethylene-3-hydroxy-1,2,3,4-tetrahydroquinolin-4-one (12) with Ethyl (Triphenylphosphoranylidene)acetate (4). The solution of compounds (**12**) (185 mg, 0.51 mmol) and (**4**) (191 mg, 0.55 mmol) in xylene (3 mL) was refluxed for 4 h. After evaporation to dryness *in vacuo* the residue was column chromatographed on silica gel (15 g) using benzene as eluent to give 144 mg (77%) of **12** and 32 mg (16%) of compound (**15**).

Reaction of 3*a*-Benzyl-6,9-dimethyl-2,3*a*,4,5-tetrahydrofuro[2,3-*c*]quinoline-2,4-dione (13) with Ethyl (Triphenylphosphoranylidene)acetate (4). The mixture of compounds (**13**) (319 mg, 1 mmol) and (**4**) (348 mg, 1 mmol) in xylene (8 mL) was refluxed for 3 h. After cooling to rt, the precipitate was filtered off with suction to give 222 mg (70%) of lactone (**14**). The filtrate was evaporated to dryness *in vacuo* and the residue was column chromatographed on silica gel (20 g). Elution with benzene provided 75 mg (19%) of yellow compound (**15**).

Preparation of 3-Benzyl-5,8-dimethyl-4-ethoxy-2(1*H*)-quinolone (16). To the solution of **3b** (576 mg, 2.0 mmol) and potassium hydroxide (199 mg, 3.55 mmol) in ethanol (15 mL), 0.38 mL (2.9 mmol) of diethyl sulfate was added. The reaction mixture was left to stand at rt for 1.5 h and subsequently warmed on the water bath for 15 min. After evaporation almost to dryness *in vacuo*, the residue was diluted with water (20 mL), made alkaline with 0.5 M NaOH and extracted three times with chloroform (30 mL). Combined chloroform fractions were evaporated to dryness and the residue was crystallized from ethyl

acetate to give 375 mg (61%) of compound (**16**). From the alkaline water solution, 209 mg (35%) of the starting **3b** was recovered after acidification with hydrochloric acid.

General Procedure for the Preparation of 3-Bromoacetoxy-1,2,3,4-tetrahydroquinoline-2,4-diones (18a,b). To the suspension of the appropriate 3-hydroxy-1,2,3,4-tetrahydroquinoline-2,4-dione (**3a,b**) (10 mmol) in benzene (60 mL), pyridine (0.81 g, 10.5 mmol) and then subsequently a solution of bromoacetyl bromide (2.22 g, 11 mmol) in benzene (10 mL) were added under stirring at rt. After additional stirring for 2 h at rt, the reaction mixture was heated to 60°C for 1 h and, after cooling, precipitated pyridine hydrobromide was filtered off with suction. The filtrate was evaporated to dryness *in vacuo* and the residue was crystallized.

General Procedure for the Preparation of 3-Triphenylphosphonioacetoxy-1,2,3,4-tetrahydroquinoline-2,4-dione bromides (19a,b). The suspension of the appropriate 3-bromoacetoxy-1,2,3,4-tetrahydroquinoline-2,4-dione (**18a,b**) (10 mmol) and triphenylphosphane (3.15 g, 12 mmol) in benzene (30 mL) was refluxed for 4-6 h. After cooling, the precipitate was filtered with suction, washed with benzene and used in further experiments without crystallization.

Preparation of 3*a*-Benzyl-9-chloro-6-methyl-2,3*a*,4,5-tetrahydrofuro[2,3-*c*]quinoline-2,4-dione (9). The solution of the bromide (**19a**) (1.4 g, 2 mmol) in chloroform (30 mL) was shaken with 0.5 M sodium hydroxide (10 mL) for 10 min. The chloroform layer was separated, washed with water, dried with anhydrous sodium sulfate and evaporated to dryness *in vacuo*. After crystallization from methanol, 0.56 g (82%) of the product (**9**) was obtained.

Preparation of 3-Benzyl-5,8-dimethyl-3-triphenylphosphoranylideneacetoxy-1,2,3,4-tetrahydroquinoline-2,4-dione (20). The solution of the bromide (**19b**) (1.2 g, 1.77 mmol) in chloroform (30 mL) was shaken with 0.5 M sodium hydroxide (10 mL) for 10 min. The chloroform layer was separated, washed with water, dried with anhydrous sodium sulfate and evaporated to dryness *in vacuo*. After crystallization from methanol, 0.75 g (71%) of the ylide (**20**) was obtained.

Preparation of 3*a*-Benzyl-6,9-dimethyl-2,3*a*,4,5-tetrahydrofuro[2,3-*c*]quinoline-2,4-dione (13) The solution of the ylide (**20**) (0.8 g, 1.34 mmol) in xylene (10 mL) was refluxed for 40 min. After cooling, the precipitated crystals were filtered off and 0.41 g (96%) of **13** was obtained.

ACKNOWLEDGEMENTS

This study was supported by the Grant Agency of the Czech Republic (Grant No. 203/97/0033) and The Ministry of Science and Technology of Slovenia. The authors are indebted to Professor O. Červinka (Prague Institute of Chemical Technology) for fruitful discussions on the reaction mechanism and to Mrs.

H. Geržová for technical help. We would like to thank Drs. Bogdan Kralj and Dušan Zigon (Mass Spectrometry Centre, Jozef Stefan Institute, Ljubljana, Slovenia) for mass spectral measurements.

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15. For the yields no referred in Table II see Experimental.

Received, 27th July, 1998