Synthesis of 3-Alkylcoumarins and 3-Alkyl-α,β-unsaturated δ-Lactones from 3-Diethylphosphonocoumarins, 3-Diethylphosphonolactones and Aldehydes

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3-Phosphonocoumarins, 3,4-Dihydrophosphonocoumarins, 3-Alkylcoumarins

The treatment of salicylaldehyde 1 and derivatives 2 – 4 with triethyl phosphonoacetate 5 in refluxing toluene using piperidine acetate and β-alanine affords 3-diethyl phosphono-2-oxo-5,6-dihydro-2H-pyranes. With aromatic aldehydes, under Wittig-Horner conditions, affords α-methylen monosubstituted δ-lactones as E-isomers, while the reaction of the Wittig-Horner compounds with aliphatic aldehydes gave α-methylen monosubstituted δ-lactones usually as mixtures of E and Z stereoisomers. As reported in previous papers [2, 3], Knoevenagel condensation catalyzed by TiCl4/pyridine, starting from β-hydroxaldehydes and CH2-acidic components, led to the direct lactonisation of 3-substituted-2-oxo-5,6-dihydro-2H-pyranes. The use of a mixture of piperidine acetate/β-alanine in the Knoevenagel condensation, starting from β-hydroxaldehydes and CH2-acidic compounds, showed excellent catalytic properties for the lactonisation [4, 5].

In this paper, we report on the synthesis of 3-diethylphosphonocoumarins 6-9 starting from salicylaldehyde 1 and derivatives 2-4 with triethyl phosphonoacetate 5, a Knoevenagel condensation, catalyzed by piperidine acetate/β-alanine and on the hydrogenation, catalyzed by platinum(IV) oxide, of the 3-diethylphosphonocoumarins 6-9 to 3-diethylphosphono-3,4-dihydrocoumarins 10-13. The treatment of the new Wittig-Horner compounds 10-13 with aromatic aldehydes 14-18 unexpectedly leads to 3-alkylcoumarins 19-24 in satisfactory yields. The reaction of 3-diethylphosphonolactones 25, 26 with isatin 27 and 5-bromoisatin 28, under similar reaction conditions, leads to 3-alkyl-α,β-unsaturated δ-lactones 29-31.

Introduction

We reported recently [1] on the synthesis of new Wittig-Horner compounds by hydrogenation of α,β-unsaturated 3-diethylphosphonolactones in presence of platinum(IV) oxide in isopropyl alcohol. We observed that the olefination of 3-diethylphosphono-2-oxo-tetrahydropyranes with aromatic aldehydes, under Wittig-Horner conditions, afforded α-methylen monosubstituted δ-lactones as E-isomers, while the reaction of the Wittig-Horner compounds with aliphatic aldehydes gave α-methylen monosubstituted δ-lactones usually as mixtures of E and Z stereoisomers. As reported in previous papers [2, 3], Knoevenagel condensation, catalyzed by TiCl4/pyridine, starting from β-hydroxaldehydes and CH2-acidic components, led to the direct lactonisation of 3-substituted-2-oxo-5,6-dihydro-2H-pyranes. The use of a mixture of piperidine acetate/β-alanine in the Knoevenagel condensation, starting from β-hydroxaldehydes and CH2-acidic compounds, showed excellent catalytic properties for the lactonisation [4, 5].

In this paper, we report on the synthesis of 3-diethylphosphonocoumarins 6-9 starting from salicylaldehyde 1 and derivatives 2-4 with triethyl phosphonoacetate 5, a Knoevenagel condensation, catalyzed by piperidine acetate/β-alanine and on the hydrogenation, catalyzed by platinum(IV) oxide, of the 3-diethylphosphonocoumarins 6-9 to 3-diethylphosphono-3,4-dihydrocoumarins 10-13. The treatment of the new Wittig-Horner compounds 10-13 with aromatic aldehydes 14-18 unexpectedly leads to 3-alkylcoumarins 19-24. The reaction of 3-diethylphosphono-δ-lactones 25, 26 with the isatin 27 and 5-bromoisatin 28 does not afford α-methylenderivatives [6] but only 3-alkyl-δ-lactones 29-31.

Results and Discussion

In connection with our synthesis of compounds with lactonic structure we have observed that the proper use of catalysts in the Knoevenagel reaction afforded the condensation of the lactonic compounds. Surprisingly, the use of TiCl4/pyridin in the reaction of β-hydroxaldehydes with triethyl phosphonoacetate led to the cyclocondensation of the lacton in satisfactory yields [2, 3], in place of the simple condensation. During the investigation of the properties of various catalysts, we have found that a mixture of piperidine acetate/β-alanine has demonstrated good catalytic properties in the condensation and direct lactonisation of β-hydroxyaldehydes with CH2-acidic compounds [4, 5]. The use of piperidine acetate/β-alanine in the Knoevenagel condensation opens a route to a new class of compounds of synthetic interest owing to their novel structure and the presence of different functional groups.

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The reaction of aromatic hydroxyaldehydes 1–4 with triethyl phosphonoacetate 5 using piperidine acetate/β-alanine in refluxing toluene affords 3-diethyl-phosphonocoumarins 6–9 in excellent yields (Scheme 1). All the structural assignments of the compounds 6–9 were made on the basis of 1H NMR analysis and EI-MS spectrometry. The doublet at $\delta = 8.5 – 8.9$ ppm with the coupling constant $\nu_{\text{HP}} = 17$ Hz, due to the vinylic proton H-4 demonstrates the cis configuration to the phosphorous [7]. The 31P NMR spectra of the compounds 6–9 show singlets shifted at $\delta = 9 – 10$ ppm and reveal a low dependence of the inductive effect at the substituents on the aromatic moiety of the coumarins. In the EI-MS spectra, molecular ions have been observed at $m/z = 282$ (6), 312 (7), 326 (8), 360, 362 (9), respectively.

The hydrogenation of 3-diethyl-phosphonocoumarins 6–9, in presence of platinum(IV) oxide in isopropyl alcohol at 130 atm and at room temperature leads to the unknown 3-diethyl-phosphono-3,4-dihydrocoumarins 10–13 in 90% yields (Schema 2). The molecular ions in the EI-MS at $m/z = 284$ (10), 314 (11), 328 (12), 364, 366 (13), respectively and the multiplet at $\delta = 4.0 – 3.5$ ppm due to the protons H-3 and H-4 in the 1H NMR spectra of 10–13 confirms the complete hydrogenation of the starting products 6–9. The strong electronic variation due to the hydrogenation at the carbons C-3 and C-4, causes in the 31P NMR spectra a chemical shift at low fields at ca. 10 ppm. Further, the hydrogenation of the carbons C-3 and C-4 determines the formation of cis, trans isomers with different chemical shifts in the 13C NMR spectra, due to the steric disposition of the group PO2C2H5; these data result in good agreement with those reported in literature [8].

Under our experimental conditions, the reaction of the new Wittig-Horner compounds with the aromatic aldehydes 14–18 in presence of sodium hydride in dry tetrahydrofuran surprisingly does not
afford the expected 3-methylenecoumarins, but produces 3-alkylcoumarins 19–24 (Scheme 3).

The formation of the compounds 19–24 can be due to the energetic instability of the exocyclic double bond in the coumarinic moiety. The migration of the exocyclic double bond leads to the more stable coumarinic structure opening so a new route for the synthesis of 3-alkylcoumarins [9, 10].

As described in a recent paper [1], the olefination of 3-phosphonolactones, under Wittig-Horner conditions, with aromatic aldehydes led exclusively to the synthesis of α-methylen monosubstituted δ-lactones in the E-form. In the attempt to synthesize α-methylene compounds, starting from 3-phosphonolactones 25, 26, under Wittig-Horner conditions, and from isatin 27 and 5-bromoisatin 28, surprisingly we have observed the formation of 3-alkyl-δ-lactones 29–31 only (Scheme 4).

On the basis of the above obtained results, we can affirm that the reaction of 3-phosphonolactones 25, 26, under Wittig-Horner conditions, with aromatic and aliphatic aldehydes, gives α-methylene monosubstituted δ-lactones only [1], while with aromatic condensed structures, 3-alkyl-δ-lactones have been obtained.

The 1H NMR spectra of the compounds 19–24 show singlets at δ = 4.0 ppm with an integral correspondent to two protons attributed to the proton H-11 and this results in good agreement with the data reported in literature [9], while the proton H-4 results covered by the aromatic protons at δ = 7.49–7.0 ppm. In the 13C NMR spectra the carbons C-11 show signals at δ = 36–30 ppm, while the signals of the aromatic carbons have been observed in the typical field of the coumarin moiety.

The compounds 19–23 in the EI-MS spectra give atypical fragment ions with high intensity due to the loss of OH radical from the molecular ion (M-17)+ caused by the resonance effect. This fragmentation results similar to that produced by the ortho effect (Fig. 1). Further, secondary fragment ions with low intensity correspondent to the loss of NO radical (M–NO)+, have been observed. The compound 21, very probably follows the routes A and B as primary fragmentation, followed by a secondary fragmentation correspondent to the loss of formaldehyde from the fragment 257 (Fig. 1). The molecular ions at m/z = 281 (19), 559, 361 (20), 286 (21), 301 (22), 331 (23), 256 (24) confirm the formation of 3-alkylcoumarins.

The 1H NMR spectra of the compounds 29–31, contain singlets at δ = 4.22 (29), 4.33 (30), 4.41 (31) attributed to the proton H-3 and in the field region
of 3-Alkylcoumarins
at δ = 6.65 ppm due to the proton H-4', respectively. The carbons C-3 and C-4' in the 13C NMR spectra show signals at δ = 48.9 (29), 49.0 (30), 48.5 (d) ppm (31) and at 154.2 (29), 154.1 (30), 154.0 ppm (d) (31), respectively. Molecular ions at m/z = 285 (29), 364 (30), 257 (31), and fragments with high intensity (100%), due to the loss of the propyl group in 29, 30 and methyl group in 31 at m/z = 242, respectively have been observed.

Experimental
Melting points were determined on a Büchi mod. 510 apparatus and are uncorrected.

The purity of the synthesized compounds was checked out by TLC on precoated silica gel aluminium sheets (Merck 60 F254). Spots were visualized under 254 nm illumination. Flash-chromatography was performed on silica gel (Kieselgel 60, 0.063–0.042 mm, Merck). The solvents used were freshly distilled before use. All the starting reactants were commercially available.

1H NMR and 13C NMR spectra (CDCl3) were recorded on a Varian Gemini-200 spectrometer. 31P NMR spectra were recorded on a Bruker Physik HX 90 R using H3PO4 85% (CDCl3) as standard. Chemical shifts are given in ppm from TMS as internal standard, and coupling constants (J) in Hz. The EI-MS spectra were measured with a VG-ZAB 2F spectrometer. The ionizing energy was 70 eV in all cases and compounds were introduced by direct insertion.

a) Synthesis of α-Diethyl-phosphonocoumarins 6–9
General procedure
0.081 Moles of 2-hydroxyaldehyde 1–4, dissolved in 100 ml of toluene, together with 0.081 moles of triethyl phosphonoacetate, 0.04 g of β-alanine and 0.4 g of piperidine acetate, were refluxed for times ranging from 8 to 15 h and the water formed was collected in a separatory funnel. The solution was then allowed to cool and treated with an aqueous saturated NaCl solution (100 ml). The organic layer was collected, dried and concentrated in vacuo. Purification by column chromatography, eluting with hexane/ethyl acetate (3:7, v/v) gav e an oil. Diethyl ether was added to the oil obtained and the crystals formed on cooling were collected by filtration.

3-Diethyl-phosphonocoumarin 6
Prepared from 10 g of salicylaldehyde 1 and 18 g of triethyl phosphonoacetate 5. The crude reaction material obtained has been chromatographed to give 19.6 g (85%) of 6 as an oil, which on standing afforded crystals, crystallized from diethyl ether (m.p.: 92 °C). C15H14OSiO2P (282.2).

31P [1H] NMR (CDCl3): δ = 10.59 (s). 1H NMR (CDCl3): δ = 1.38 (t; J = 7.5 Hz, 6H), 3.75 (s; 3H), 4.80 (d; J = 17.2 Hz, 1H, H-4). - EI-MS (70 eV): m/z = 282 (M, 22%)*, 254 (M-28, 4%)*, 237 (M-45, 7%)*, 224 (M-58, 7%)*, 209 (M-45-28, 37%)*, 197 (M-C8H10=CO, 37%)*, 180 (M-C4H10=CO2, 33%)*, 174 (C8H7PO4, 100%)*, 146 (C4H3PO4, 33%)*, 81 (C3H6, 33%)*.

3-Diethyl-8-methoxy-phosphonocoumarin 7
Prepared from 12.3 g of 3-methoxysalicylaldehyde 2 and 18 g of 5. The crude reaction material obtained has been chromatographed to give 17.6 g (70%) of 7 as an oil, which on standing afforded crystals, crystallized from diethyl ether (m.p.: 87 °C). C13H15OSiO2P (312.3).

31P [1H] NMR (CDCl3): δ = 10.78 (s). 1H NMR (CDCl3): δ = 1.40 (t; J = 7.5 Hz, 6H), 4.0 (s; 3H), 4.40 (q; J = 8.0 Hz, 4H), 7.50 (arom.-H, 3H), 8.75 (d; J = 17.2 Hz, 1H, H-4). - EI-MS (70 eV): 312 (M, 40%)*, 284 (M-28, 4%)*, 267 (M-45, 6%)*, 239 (M-56, 32%)*, 203 (C8H7PO4, 100%)*.

3-Diethyl-8-ethoxy-phosphonocoumarin 8
Prepared from 13.4 g of 3-ethoxysalicylaldehyde 3 and 18 g of 5. The crude reaction material obtained has been chromatographed to give 22.4 g (85%) of 8 as an oil, which on standing afforded crystals, crystallized from diethyl ether (m.p.: 94 °C). C14H17OSiO2P (326.2).

31P [1H] NMR (CDCl3): δ = 10.42 (s). 1H NMR (CDCl3): δ = 1.25, 1.20 (t; J = 7.0 Hz, 9H), 4.10–4.55 (m; 4H), 7.35 (arom.-H, 3H), 8.70 (d; J = 17.0 Hz, 1H, H-4). - EI-MS (70 eV): m/z = 326 (M, 100%)*, 298 (M-28, 16%)*, 281 (M-45, 8%)*, 270 (M-56, 24%)*, 252 (M-45–29, 46%)*, 242 (M-56–28, 67%)*, 217 (C8H7PO4, 86%)*, 189 (C4H3PO4, 54%)*, 162 (C3H6PO4, 21%)*.

6-Bromo-3-diethyl-phosphonocoumarin 9
Prepared from 16.3 g of 5-bromosalicylaldehyde 4 and 18 g of 5. The crude reaction material obtained has been chromatographed to give 26.3 g (90%) of 9 as an oil, which on standing afforded crystals, crystallized from diethyl ether (m.p.: 103 °C). C13H14BrSiO2P (361.12).

31P [1H] NMR (CDCl3): δ = 9.81 (s; 1P). 1H NMR (CDCl3): δ = 1.50 (t; J = 7.5 Hz, 6H), 4.50 (q; J = 8.0 Hz, 4H), 7.70–8.33 (arom.-H, 3H), 8.90 (d; J =
17.0 Hz, 1H, H-4). - EI-MS (70 eV): m/z = 360, 362 (M, 26%), 334 (M-28, 6%), 290 (M-28-CO2, 35%), 262 (M-CO2, 56, 19%), 251 (C6H5PO4Br, 100%), 167 (C6H5Br, 22%).

b) Synthesis of 3-Diethyl-phosphono-3,4-dihydrocoumarins 10–13

General procedure

A mixture of 0.05 moles of a-diethyl-phosphono-coumarin 6–9, 300 ml of isopropyl alcohol and 0.5 g of platinum oxide was stirred in an atmosphere of hydrogen, at 130 atm and at room temperature for 12 h at the end of which time gas uptake had ceased. The catalyst was removed by filtration of the reaction mixture. The filtrate was evaporated under reduced pressure and the residue was used without further purification.

3-Diethyl-phosphono-3,4-dihydrocoumarin 10

Prepared from 14.1 g of 6 to give 13.6 g (96%) of 10. C19H16BrO5P (384.2).

31P [1H] NMR (CDCl3): δ = 19.80 (s; 1P). - 1H NMR (CDCl3): δ = 1.05 (t; J = 7.5 Hz, 3H), 1.30 (t; J = 7.5 Hz, 3H), 3.35 (m; 2H), 3.7–4.0 (m; 3H, H-3, H-4), 4.15 (q; J = 8.0 Hz, 2H), 7.09–7.25 (arom.-H, 3H) - EI-MS (70 eV): m/z = 328 (M, 20%), 299 (M-29, 52%), 271 (M-57, 6%), 191 (M-C6H5PO4, 100%), 162 (M-138–29, 21%), 138 (C6H5PO3, 13%), 133 (15%), 122 (8%), 121 (14%), 110 (16%), 106 (13%), 80 (8%), 77 (15%), 65 (13%).

3-Diethyl-phosphono-8-ethoxy-3,4-dihydrocoumarin 12

Prepared from 16.3 g of 8 to give 15.6 g (95%) of 12. C18H15BrO3P (363.2).

31P [1H] NMR (CDCl3): δ = 19.95 (s; 1P). - 1H NMR (CDCl3): δ = 1.35 (t; J = 7.5 Hz, 3H), 2.90–3.55 (m; 3H, H-3, H-4), 4.15 (q; J = 8.0 Hz, 2H), 6.70–7.15 (arom.-H, 3H) - EI-MS (70 eV): m/z = 362, 364 (M, 5%), 335 (M-28+H, 4%), 317 (M-CHO2, 7%), 289 (M-28-CHO2, 12%), 261 (M-56-HCO2, 9%), 225 (M-C6H5PO4, 24%), 138 (C6H5PO3, 100%), 111 (C6H5PO3, 64%), 82 (21%), 63 (12%).

c) Synthesis of 3-AlkyIcoumarins 19–24 and 3-Alkyl lactones 29–31

General procedure

To a stirred suspension of 0.01 moles of sodium hydride (96%) in 50 ml of dry tetrahydrofuran, under nitrogen, at room temperature, was added dropwise a solution of 0.01 moles of a-diethyl-phosphono-3,4-dihydrocoumarin 10–13 and a-diethyl-phosphonolactones 25, 26 in 20 ml of dry THF. Upon stirring at 20 °C for 30 min, the solution was cooled at 0°C and 0.01 moles of the appropriate aldehyde 14–18 and isatin 27 and 5-bromoisatin 28 were added. After the addition, the mixture was stirred at room temperature for 18 h, and then washed with saturated NaCl solution and extracted three times.

Table I. 13C NMR chemical shifts (δ ppm) in CDCl3 of the partial structures of the compounds 6–12.

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* The aromatic C-atoms showed signals in the aromatic region and haven’t been reported.
times with ether. The organic extracts were combined, dried (Na$_2$SO$_4$), filtered and concentrated \textit{in vacuo}. The residue was purified by chromatography (SiO$_2$; ethyl acetate/hexane).

3-[(4-Nitrophenyl)methyl]-2H-1-benzopyran-2-one \textit{19}

Prepared from 3 g of 10 and 1.5 g of $p$-nitrobenzaldehyde \textit{14}. The crude reaction material obtained has been chromatographed (ethyl acetate/hexane 2:8) to give 2 g of \textit{19} (71%) as a pale yellow oil, which on standing afforded crystals (m.p.: 105 °C). C$_{16}$H$_{14}$NO$_4$ (281.3).

$^1$H NMR (CDCl$_3$): $\delta$ = 3.98 (s; 2H, H-11), 7.24–7.49 (arom.-H, 7 H), 8.20 (d; $J$ = 8, 8 Hz, 2H). - EI-MS (70 eV): $m/z$ = 281 (M, 100%), $^2$84 (M–OH, 23%), 270 (M–HNO, 33%), 256 (M–OH–28, 6%), 254 (M–HNO, 10%), 242 (M–HNO–CO, 10%), 226 (M–HNO–CO$_2$–40%), 189 (M–CH$_3$NO$_2$, 17%), 141 (C$_{11}$H$_9$, 97%), 83 (50%).

6-Bromo-3-[(4-nitrophenyl)methyl]-2H-1-benzopyran-2-one \textit{20}

Prepared from 3.62 g of 13 and 1.5 g of $p$-nitrobenzaldehyde \textit{14}. The crude reaction material obtained has been chromatographed (ethyl acetate/hexane 2:8) to give 2 g of \textit{20} (71%) as a pale yellow oil, which on standing afforded crystals (m.p.: 105 °C). C$_{16}$H$_{10}$BrNO$_4$ (360.2).

$^1$H NMR (CDCl$_3$): $\delta$ = 4.00 (s; 2H, H-11), 7.51–7.70 (arom.-H, 6H), 8.12 (d; $J$ = 8.5 Hz, 2H, arom.-H). - EI-MS (70 eV): $m/z$ = 359, 361 (M, 100%), 344 (M–OH, 54%), 329 (M–NO, 10%), 314 (M–HNO$_2$, 29%), 284 (M–HNO–CO, 4%), 205 (M–NO–CO–Br, 38%), 176 (30%), 151 (13%), 89 (29%), 76 (27%).

3-[(2-Naphthyl)methyl]-2H-1-benzopyran-2-one \textit{21}

Prepared from 2.84 g of 10 and 1.67 g of 2-naphthaldehyde \textit{15}. The crude reaction material obtained has been chromatographed (ethyl acetate/hexane 3:7) to give 1.77 g of \textit{21} (63%) as white crystals (m.p.: 105 °C). C$_{20}$H$_{14}$O$_2$ (286.3).

$^1$H NMR (CDCl$_3$): $\delta$ = 4.05 (s; 2H, H-11), 7.15–7.90 (arom.-H, 12 H). - EI-MS (70 eV): $m/z$ = 286 (M, 100%), $^2$69 (M–17, 31%), $^3$257 (M–29, 35%), $^4$228 (M–58, 11%), $^5$131 (M–CHO–C$_{10}$H$_6$, 11%).

8-Ethoxy-3-[(5-nitrothiophenyl)methyl]-2H-1-benzopyran-2-one \textit{23}

Prepared from 5 g of 12 and 2.3 g of 5-nitro-2-thiophene-carboxaldehyde \textit{17}. The crude reaction material obtained has been chromatographed (ethyl acetate/hexane 3:7) to give 2.71 g of \textit{23} (82%) as a pale yellow oil, which on standing afforded crystals (m.p.: 132 °C). C$_{16}$H$_{13}$NO$_5$S (331.3).

$^1$H NMR (CDCl$_3$): $\delta$ = 1.49 (t; $J$ = 7.5 Hz, 3H), 4.06 (s; 2H, H-11), 4.15 (q; $J$ = 8.0 Hz, 2H), 7.90–7.28 (arom.-H, 6H). - EI-MS (70 eV): $m/z$ = 331 (M, 100%), 314 (M–17, 27%).

3-[(3'-Methylthiophenyl)methyl]-2H-1-benzopyran-2-one \textit{24}

Prepared from 3 g of 10 and 1.3 g of 3-methyl-2-thiophene-carboxaldehyde \textit{18}. The crude reaction material obtained has been chromatographed (ethyl acetate/hexane 8:2) to give 1.8 g of \textit{24} (70%) as a pale yellow oil, which on standing afforded crystals (m.p.: 130 °C). C$_{15}$H$_{12}$O$_2$S (256.3).

$^1$H NMR (CDCl$_3$): $\delta$ = 2.16 (s; 3H, H-11), 6.89 (d; $J$ = 5.1 Hz, 1H), 7.12–7.50 (arom.-H, 6H). - EI-MS (70 eV): $m/z$ = 256 (M, 78%), $^2$41 (M–15, 33%), 159 (M–97, 17%), 97 (C$_{11}$H$_9$, 100%).

Table II. $^{13}$C NMR chemical shifts (δ ppm) in CDCl$_3$, of the partial structures of the compounds \textit{19}–\textit{24}.

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* The aromatic C-atoms showed signals in the aromatic region and haven’t been reported.
3-(5'-Methyl-5'-propyl-2'-oxo-5',6'-dihydro-2'H-pyranyl)-indol-2-(3H)-one 29

Prepared from 0.4 g of NaH 60%, 2.92 g of phosphonate and from 1.47 g of isatin 27. The crude reaction material obtained has been chromatographed (ethyl acetate/hexane 1:1) to give 0.5 g of 29 (17.6%) as a viscous oil. C_{17}H_{19}N_{2}O_{2} (285.3).

^1H NMR (CDCl$_3$): $\delta$ = 8.5 ppm (s; 1H, NH), 7.55 - 6.90 (m; arom.-H, 4 H), 6.65 (s; 1H, H-4'), 4.45 (s; 1H, H-3), 4.22, 4.15 (ABq; $J$ = 11.0 Hz, 2H, H-6'), 1.45 - 1.20 (m; propyl-H, 4H), 1.12 (s; CH$_3$-5'), 0.95 (t; $J$ = 7.0 Hz, CH$_3$-propyl). – EI-MS (70 eV): m/z = 285 (M, 64%), 270 (M - CH$_3$, 9%), 242 (M - C$_3$H$_7$, 100%), 224 (M - C$_3$H$_7$ - 18, 18%), 199 (M - C$_3$H$_2$O$_3$, 34%), 181 (M - C$_3$H$_2$O$_3$ - 18, 32%), 154 (C$_9$H$_14$O$_2$, 11%), 131 (M - C$_9$H$_14$O$_2$, 20%).

5-Bromo-3-(5'-methyl-5'-propyl-2'-oxo-5',6'-dihydro-2'H-pyranyl)-indol-2-(3H)-one 30

Prepared from 0.4 g of NaH 60%, 2.92 g of phosphonate and from 2.26 g of 5-bromoisatin 28. The crude reaction material obtained has been chromatographed (ethyl acetate/hexane 1:1) to give 1.1 g of 30 (55%) as a viscous oil. C$_{17}$H$_{18}$BrN$_2$O$_2$ (364.2).

$^1$H NMR (CDCl$_3$): $\delta$ = 7.79 ppm (s; 1H, NH), 7.35 (dd; $J$ = 8.2, 2.0 Hz, 1H, H-6), 6.77 (d; $J$ = 4.5 Hz, 1H, arom.-H), 6.69 (s; 1H, H-4'), 4.33 (s; 1H, H-3), 4.21, 4.10 (ABq; $J$ = 11.0 Hz, 2H, H-6'), 1.57 - 1.33 (m; 4H, propyl-H), 1.16 (s; CH$_3$-5'), 0.97 (t; $J$ = 7.0 Hz, CH$_3$-propyl). – EI-MS (70 eV): m/z = 364 (M, 46%), 349 (M - CH$_3$, 7.7%), 321 (M - C$_3$H$_7$, 100%), 303 (M - C$_3$H$_7$ - 18, 19%), 278 (M - C$_3$H$_2$O$_2$, 27%), 275 (M - C$_3$H$_2$O$_2$ - 18, 48%), 260 (275 - 15, 21%)$^*$, 210 (M - C$_9$H$_{14}$O$_2$, 15%), 154 (C$_9$H$_{14}$O$_2$, 19%).

5-Dimethyl-3-(5'-methyl-5'-propyl-2'-oxo-5',6'-dihydro-2'H-pyranyl)-indol-2-(3H)-one 31

Prepared from 0.4 g of NaH 60%, 2.92 g of phosphonate and from 1.47 g of isatin 27. The crude reaction material obtained has been chromatographed (ethyl acetate/hexane 1:1) to give 0.98 g of 31 (38%). C$_{15}$H$_{15}$N$_2$O$_2$ (257.2).

$^1$H NMR (CDCl$_3$): $\delta$ = 7.75 ppm (s; 1H, NH), 7.22, 6.86 (arom.-H, 4 H), 6.63 (s; 1H, H-4'), 4.41 (s; 1H, H-3), 4.12 (s; 2H, H-6'), 1.20 - 1.18 (s; 2 CH$_3$-5'), – EI-MS (70 eV): m/z = 257 (M, 100%), 242 (M - CH$_3$, 94%), 199 (M - C$_3$H$_2$O$_2$, 82%), 131 (M - C$_3$H$_{10}$O$_2$, 43%).

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Table III. $^{13}$C NMR chemical shifts ($\delta$ ppm) in CDCl$_3$ of the partial structures of the compounds 29–31.

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<th>C-Atom</th>
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<td>CH$_2$-prop.</td>
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* The aromatic C-atoms showed signals in the aromatic region and haven’t been reported.

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