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On the Reaction of Isatin with Cyanomethylene(triphenyl)-phosphorane. A Nucleophilic Attack of Alkyl Phosphites on the Carbon–Carbon Double Bond of (*E*)-Oxindolylideneacetonitrile

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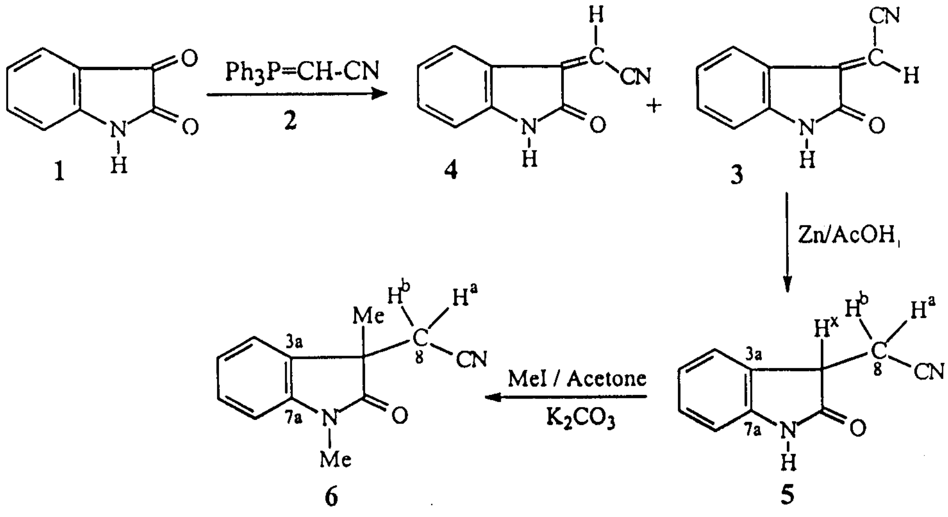
Abstract—The reaction of cyanomethylene(triphenyl)phosphorane (**2**) with isatin (**1**) in dry benzene at room temperature for 1 h led to the formation of (1,2-dihydro-2-oxo-3H-indol-3-yl)acetonitrile as a mixture of *E*- and *Z*-stereo isomers **3** and **4**. Trialkyl phosphites **7** reacted with (*E*)-nitrile **3** in dry benzene at 70°C for about 10 h to give the phosphonates **8** as two isomers together with the unexpected spiro products of isomers **9**. When the (*E*)-nitrile **3** was allowed to react with dialkyl phosphites (**11**) without solvents at 100°C for about 30 h, a mixture of the phosphonate derivatives **8** and one isomer of the dimeric structure **9** were obtained. The reaction mechanisms are considered and the structural assignments of the new compounds are based on chemical and spectroscopic evidence. © 2000 Elsevier Science Ltd. All rights reserved.

Introduction

Pietra[1] reported that the reaction of isatin (**1**) with cyanoacetic acid afforded oxindolylidenecyanoacetic acid, which upon heating with pyridine, lost carbon dioxide with the formation of oxindolylideneacetonitrile. This product was separated as two isomers (***E***)-(**3**) and (***Z***)-(**4**) by Long et al.[2] Now, we report the one-step synthesis of the two forms via Wittig reaction between isatin (**1**) and cyanomethylene(triphenyl)phosphorane (**2**). Also, our studies include the reaction of alkyl phosphites with (*E*)-oxindolylideneacetonitrile (**3**).

Results and Discussion

The reaction of isatin (**1**) with cyanomethylene(triphenyl)phosphorane (**2**) in dry benzene at room temperature for 1 h



Scheme 1.

Keywords: isatin; cyanomethylene(triphenyl)phosphorane; (*E*)-oxindolylideneacetonitrile.

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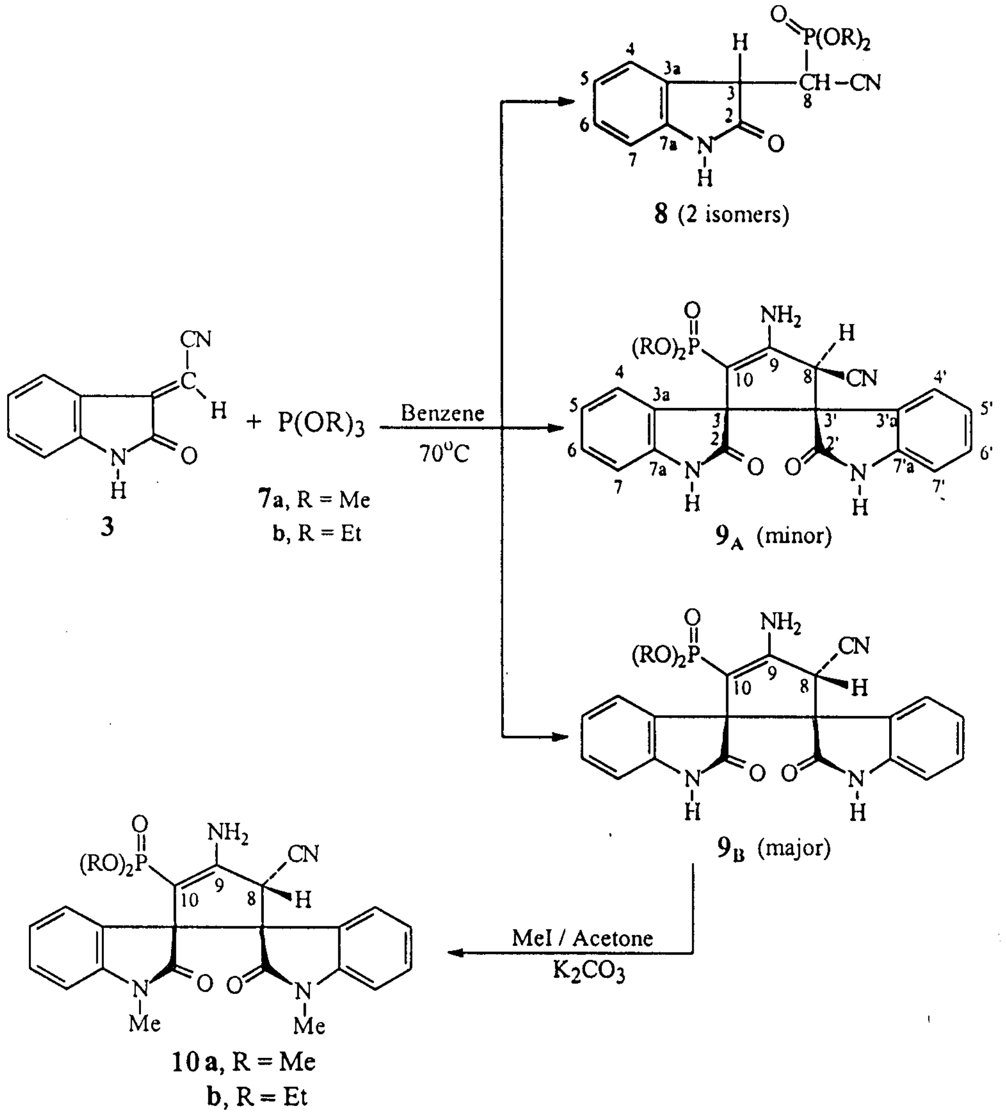


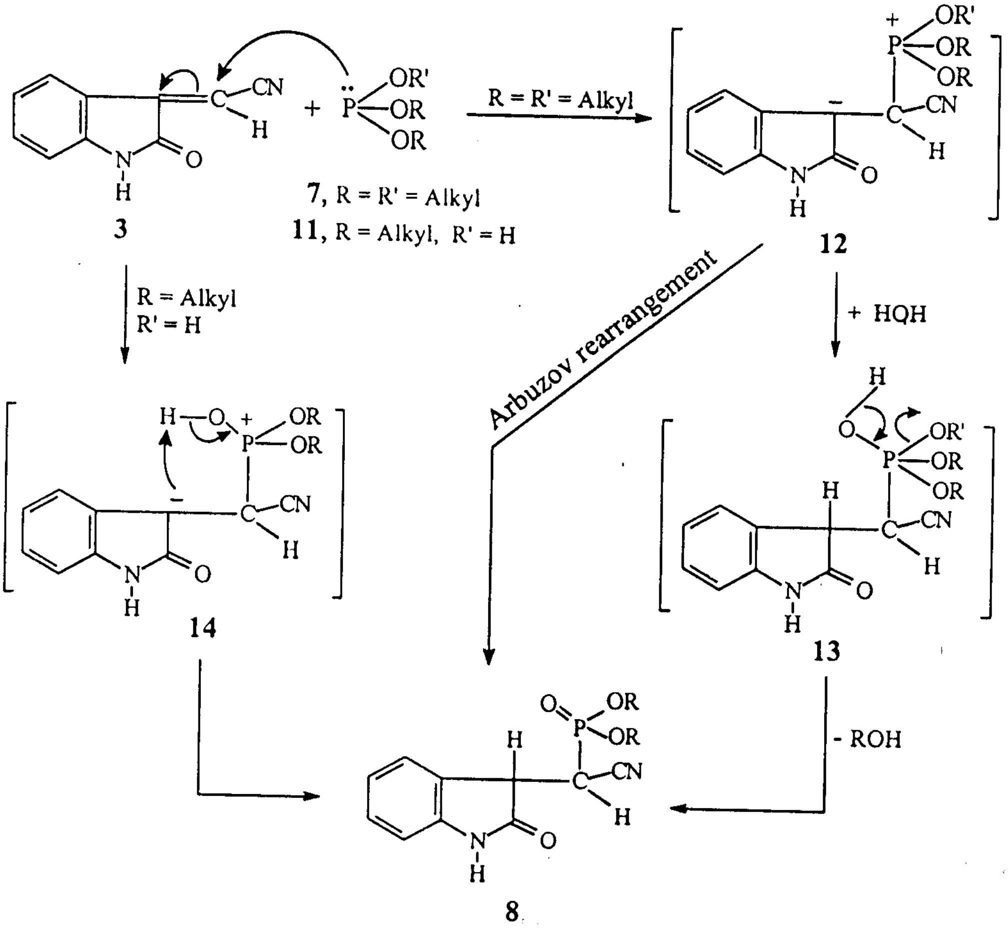
Scheme 2.

led to the formation of orange yellow crystals of (*E*)-(1,2-dihydro-2-oxo-3H-indol-3-yl)acetonitrile (**3**) (79%) and (*Z*)-(1,2-dihydro-2-oxo-3H-indol-3-yl)acetonitrile (**4**) (3%) (Scheme 1). These two isomers were separated by column chromatography on silica gel and identified by spectral data and elemental analyses. The ^{1}H NMR spectra of the two isomers in DMSO-d_6 showed the resonance of the olefinic proton of **3** (δ 6.51) at higher field than of **4** (δ 6.94). The aromatic proton at C-4 in compound **3** (δ 7.85) is deshielded more than that of compound **4** (δ 7.70) due to the nitrile group.[3] ^{1}H NMR measurements showed equilibration of the pure (*Z*)-nitrile **4** in DMSO-d_6 to a mixture of both isomers **4** and **3** in 44/56 ratio after about two weeks.

The double bond of **3** is reduced with zinc dust in boiling acetic acid to give (2,3-dihydro-2-oxo-1H-indol-3-yl)acetonitrile (**5**) in quantitative yield (Scheme 1). The ^{1}H NMR spectrum of **5** ($CDCl_3$+drop DMSO-d_6) included three doublets of doublets for *ABX* system of the CH_2CH side chain (J_{AB}=17 Hz, J_{AX}=8.4 Hz, J_{BX}=5.0 Hz).[4] Also its structure was supported by ^{13}C NMR results (cf. Experimental).

Reaction of compound **5** with methyl iodide in presence of acetone and anhydrous potassium carbonate afforded an oily product could not be solidified of (2,3-dihydro-1,3-dimethyl-2-oxo-1H-indol-3-yl)acetonitrile (**6**) (Scheme 1). The structure of compound **6** was elucidated by correct elemental analyses, molecular weight determination (MS) and compatible spectroscopic results. Its IR spectrum disclosed the absence of absorption band of NH group. The ^{1}H NMR spectrum, of **6** showed two singlets for the C-Me and *N*-Me groups and AB pattern for the CH_2 group (J_{AB}=16.8 Hz).[5] Also, further evidence supporting structure **6** is ^{13}C NMR spectral data (cf. Experimental).

Trialkyl phosphites (**7**) reacted with (*E*)-nitrile (**3**) in dry benzene at 70°C for about 10 h to give dialkyl [cyano(2,3-dihydro-2-oxo-1H-indol-3-yl)methyl]phosphonate (**8**) as two isomers together with the unexpected product of isomers **9**$_A$ and **9**$_B$ (Scheme 2). These compounds were separated by column chromatography using silica gel with *n*-hexane/acetone as eluent. The colourless crystalline product **8** was found to be a mixture of two diastereomeric forms **8**$_A$ and **8**$_B$. We separated small amounts of one isomer



Scheme 3.

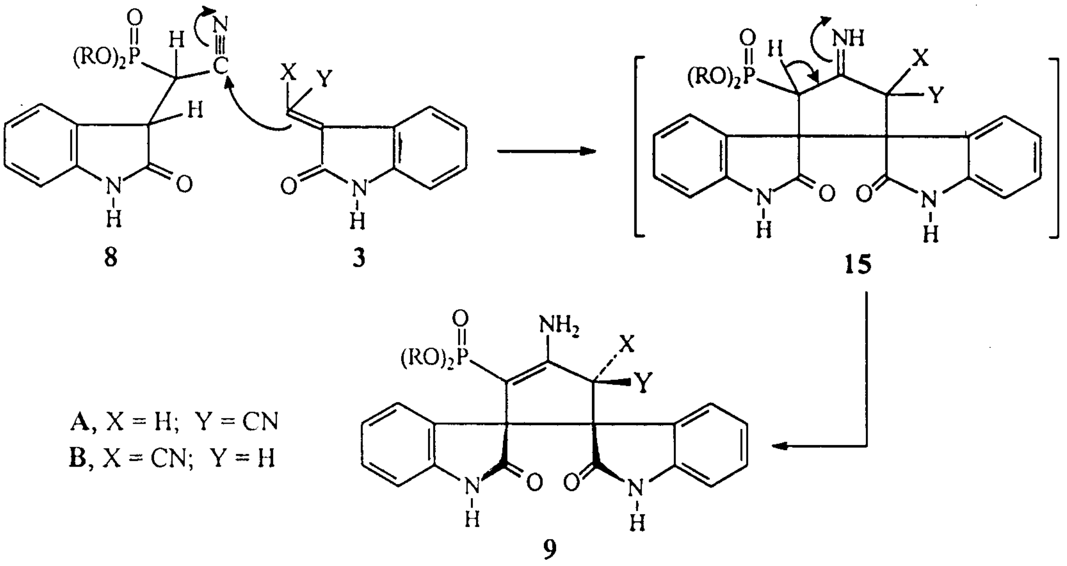
by column chromatography with identification by ^{1}H NMR, whereas the other isomer **8**$_B$ could not be isolated. The suggested structures of the phosphonates **8**$_A$ and **8**$_B$ were supported by ^{1}H and ^{13}C NMR chemical shifts. The ^{1}H NMR spectrum of isomer **8a**$_A$ showed two doublets of doublets at δ 4.17 ($^3J_{HP}$=25.4 Hz, J_{HH}=3.4 Hz) and δ 4.49 ($^2J_{HP}$=23.6 Hz, J_{HH}=3.4 Hz) for H-3 and H-8, respectively, whereas these two protons in the other isomer **8a**$_B$ appeared at δ 4.05 ($^3J_{HP}$=16.6 Hz, J_{HH}=2.4 Hz) and δ 4.43 (J_{HP}=24.6 Hz, J_{HH}=2.6 Hz) as two doublets of doublets. Moreover, ^{13}C NMR spectrum of **8a**$_A$ exhibited a doublet at δ 28.9 ($^1J_{PC}$=141.6 Hz) corresponding to C-8 and for the other isomer **8a**$_B$ a doublet at δ 29.2 ($^1J_{PC}$=145.3 Hz).

The ^{1}H NMR spectrum of the pure isomer **8**$_A$ in DMSO-d_6 changed with time, showing after about 3 h the two equilibrating species **8**$_A$ and **8**$_B$ in a 67/33 ratio, which became 57/43 ratio after 24 h.

The proposed mechanism for the formation of phosphonates **8** from the reaction of (*E*)-nitrile **3** with trialkyl phosphites **7** is depicted in Scheme 3. This involves primary nucleophilic attack by phosphite-phosphorus on the exocyclic methide carbon in **3** to yield the dipolar species **12**. The intermediate **12** undergoes addition of water due to the non-avoidable moisture to give **13**, which eliminates alcohol to form the phosphonate structure **8**. Another proposed pathway for formation of **8** could take place via nucleophilic displacement of R′ in the intermediate **12** (Arbuzov-type reaction).

The two isomers **9**$_A$ and **9**$_B$ were separated as colourless crystals and their structures were established by spectroscopic techniques as well as elemental analyses and molecular weight determination (MS). Their IR spectra showed two absorption bands near 3419 and 3316 cm^{-1} for asymmetric and symmetric NH$_2$ stretching frequencies.[6] The ^{1}H NMR spectra of both isomers **9**$_A$ and **9**$_B$ contained a singlet at δ 6.30 corresponding to the $-$NH$_2$ group and another two singlets at δ 10.69, 11.03 for the two indole *N*–H protons, which are exchangeable with D$_2$O. By comparison of the ^{1}H NMR spectra of the two isomers the chemical shift of H-4′ in **9a**$_A$ (δ 8.21) is downfield about 0.59 ppm from that of **9a**$_B$ (δ 7.62). This reflects the deshielding effect of the nitrile group on H-4′.[3] Also, H-8 in **9**$_A$ and **9**$_B$ is a singlet at δ 3.94, 4.27, respectively. The downfield effect of H-8 in case of **9**$_B$ than **9**$_A$ can be attributed mainly to the effect of neighboring carbonyl functions (C-2′ and C-2). These data were supported by ^{13}C NMR results (cf. Experimental) which showed the appearance C-10 as a doublet at δ 86.1 ($^1J_{PC}$=199.0 Hz)[7,8] for the isomer **9a**$_A$ and for the other isomer **9a**$_B$, the doublet at δ 87.1 ($^1J_{PC}$=195.3 Hz).

The postulated mechanism for the formation of the spiro-products **9**$_{A,B}$ illustrated in Scheme 4 shows the reaction of

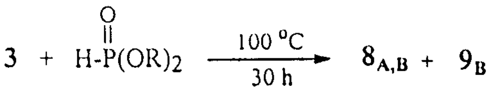


Scheme 4.

the phosphonate **8** with (*E*)-nitrile **3** involving the spiro-intermediate **15**. The latter collapses to the final isolable isomers $\mathbf{9_A}$ and $\mathbf{9_B}$.

Treatment of the major isomers $\mathbf{9a_B}$ and $\mathbf{9b_B}$ with methyl iodide in presence of acetone and anhydrous potassium carbonate led to the formation of colourless crystals of compounds **10a** and **10b**, respectively, as shown in Scheme 2. The structure of compounds **10a** and **10b** was elucidated by correct elemental analyses, molecular weight determination (MS) and compatible spectroscopic results. The IR spectra of these adducts exhibited strong absorption bands around 3462 and 3315 cm^{-1}, corresponding to NH_2 group. Their ^1H NMR spectra revealed the presence of two singlets at δ 3.20, 3.23, for the two *N*-Me groups, which appeared in ^{13}C NMR spectra at δ 26.7 and 27.0.

When the (*E*)-nitrile **3** was allowed to react with dialkyl phosphites (**11**) without solvents at 100°C for about 30 h, a mixture of the phosphonate derivatives $\mathbf{8_{A,B}}$ (as two isomers) and only one isomer of the dimeric structure $\mathbf{9_B}$ were obtained. These products were separated by column chromatography as colourless crystals. The structures were verified by mp, mixed mp and comparison of IR and ^1H NMR spectra with authentic samples (vide supra).

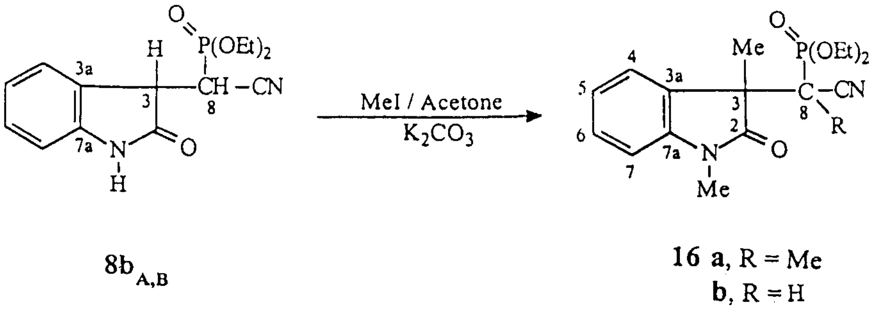


$$3 + \mathrm{H\text{-}\overset{\overset{\textstyle O}{\|}}{P}(OR)_2} \xrightarrow[30\ h]{100\ ^\circ C} 8_{A,B} + 9_B$$

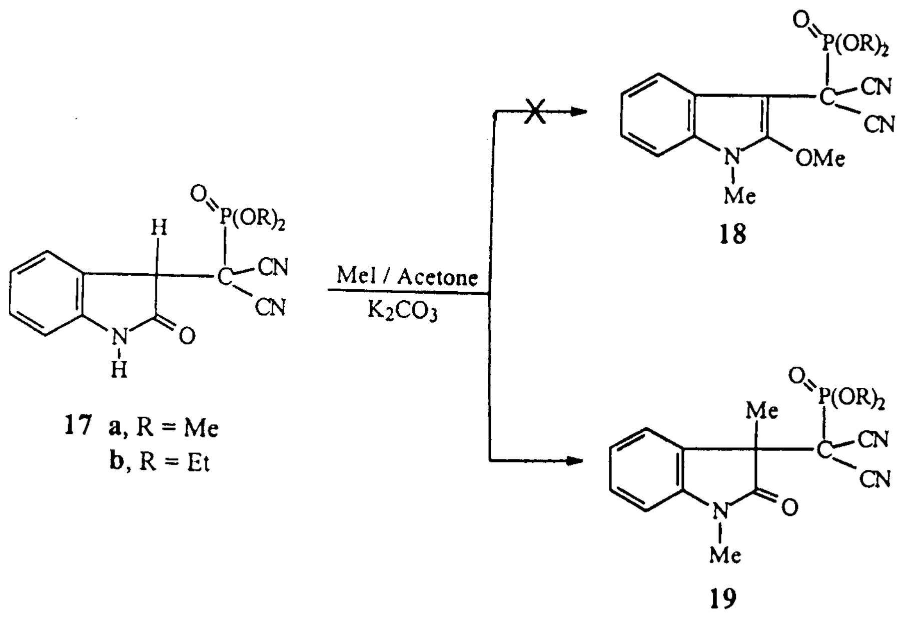
11 a, R = Me
b, R = Et

The formation of the phosphonates $\mathbf{8_{A,B}}$ from the reaction of (*E*)-nitrile **3** with phosphites (**11**) can be explained in Scheme 3 by initial nucleophilic attack of the phosphite-phosphorus on the exocyclic methide-carbon in **3** to yield the phosphonium species **14**, which afforded the phosphonates $\mathbf{8_A}$ and $\mathbf{8_B}$ as two isomers.

Methylation of the isomeric mixture $\mathbf{8b_A}$ and $\mathbf{8b_B}$ with methyl iodide in presence of acetone and anhydrous potassium carbonate led to the formation of a mixture of diethyl [1-cyano-1-(2,3-dihydro-1,3-dimethyl-2-oxo-1H-indol-3-yl)ethyl]phosphonate (**16a**) and diethyl [cyano (2,3-dihydro-1,3-dimethyl-2-oxo-1H-indol-3-yl)methyl]-phosphonate (**16b**). The colourless crystals of compounds **16a** and **16b** were separated by column chromatography on silica gel and their structures were established by



Scheme 5.



Scheme 6.

spectroscopic results. The ^{1}H NMR spectrum of the adduct **16a** showed two singlets at δ 1.62, 3.19, corresponding to Me at C-3 and *N*-Me, respectively, whereas the Me at C-8 appeared as a doublet at δ 1.95 (J_{HP}=15.4 Hz but in case of product **16b**, the ^{1}H NMR spectum revealed the presence of a singlet at δ 3.22, due to *N*-Me and two doubletes at δ 1.57 ($^4J_{\mathrm{HP}}$=2.0 Hz) and δ 3.64 ($^2J_{\mathrm{HP}}$=23.0 Hz), for Me at C-3 and H-8, respectively. These data were supported by ^{13}C NMR results (cf. Experimental). The observed transformation of $\mathbf{8_B}$ to $\mathbf{8_A}$ in DMSO-d_6 explains the highly predominant stability of the latter species. This may indicate that the formation of **16a** and **16b** via thermal methylation reaction of the corresponding diastereoisomeric mixture of **8** must originate from the more stable isomer $\mathbf{8_A}$ (Scheme 5).

Recently, it has been reported[9] that the methylation of dimethyl [dicyano(2,3-dihydro-2-oxo-1H-indol-3-yl)methyl]-phosphonate (**17a**) with methyl iodide in presence of acetone and anhydrous potassium carbonate gave a product of structure **18a** (Scheme 6). On repetition of the same experiment, we have found the reaction was over after about 30 min (examined by TLC) to give dimethyl [dicyano(2,3-dihydro-1,3-dimethyl-2-oxo-1H-indol-3-yl)methyl]phosphonate (**19a**) and not the reported structure **18a** (Scheme 6). On increasing the reaction time, compound **19a** in solution is transformed into a product insoluble in acetone and agglomerated with potassium carbonate. For this reason, we could not isolate it in the pure form. The assigned structure of **19a** was established from elemental analyses and spectral properties. The IR spectrum shows a strong absorption band characteristic for the amidic carbonyl at 1718 cm^{-1} and other two bands at 1267, 1031 cm^{-1}, corresponding to P═O and P-O-Alkyl,[6] respectively. However, the spectrum does not exhibit the expected band around 2200 cm^{-1}, due to the nitrile stretching absorption. This observation is not unusual and similar to other previously reported compounds containing cyano group attached to saturated carbon.[10–13] The ^{1}H NMR spectrum shows two singlets at δ 1.90, for the Me at C-3 and at δ 3.31, due to the *N*-Me. Two doublets at δ 3.81, 3.89 (J_{HP}=11.0 Hz) correspond to the methoxyl groups attached to phosphorus atom.

Also, the phosphonate **19b** was obtained from the reaction of compound **17b** with methyl iodide under the same experimental conditions described above for **17a**. Its ^{1}H NMR spectrum is compatible with structure **19b** and shows the presence of singlets, for the Me at C-3 and the *N*-Me.

Conclusion

The above results demonstrate a convenient new route and direct approach for preparing oxindolylideneacetonitrile (**3**) and (**4**) from the reaction of isatin (**1**) with cyanomethylene-(triphenyl)phosphorane (**2**). Also, the reaction of (*E*)-nitrile (**3**) with alkyl phosphites gave the phosphonates **8** as two isomers with unexpected spiro products **9**.

Experimental

Melting points were determined on electrical digital-melting-point apparatus and are uncorrected. The IR spectra were recorded in KBr disks, on a Jasco Fourier Transform Infrared spectrophotometer Model FT/IR-3000E. The NMR spectra were recorded on a Varian Gemini 200 spectrometer for ^{1}H operating at 200 MHz and on a Jeol Ex-270 spectrometer for ^{13}C operating at 67.5 MHz. Chemical shifts are given in positive values downfield from internal tetramethylsilane (TMS). The mass spectra (MS) were determined at 70 eV on a Finnigan MAT SSQ 7000 spectrometer.

(*E*)- and (*Z*)-(1,2-Dihydro-2-oxo-3*H*-indol-3-yl)acetonitriles (3 and 4). A mixture of isatin (**1**) (1.47 g, 10 mmol) and cyanomethylene(triphenyl)phosphorane (**2**)[14] (3.06 g, 10.2 mmol) in dry benzene (15 mL) was stirred at room temperature. After 5 min, the isatin dissolved due to the exothermic reaction with the formation of orange yellow precipitate. Stirring was continued for 1 h. Then, the solid product was filtered off, washed with dry benzene and crystallized from benzene to give the (*E*)-nitrile (**3**) (0.50 g), mp 206–207°C (lit.[2] 202–203°C), [Found C, 70.50; H, 3.63; N, 16.52. $C_{10}H_6N_2O$ requires C, 70.58; H, 3.56; N, 16.46%], ν_{max} cm^{-1} 3160 (NH); 2218 (C≡N); 1718 (C=O); 1610 (C=C), δ_H (200 MHz, DMSO-d_6) 6.51 (s, =CH); 6.92 (d, J_{HH}=7.6 Hz, H-7); 7.10, 7.43 (2t, J_{HH}=7.6 Hz, H-5, H-6); 7.85 (d, J_{HH}=7.6 Hz, H-4); 10.88 (s, NH), *m*/*z* 170 (M^+, 100%), 142 (36), 115 (29), 88 (5), 75 (2), 63 (3) and 52 (4).

The benzene filtrate was evaporated to dryness on silica gel and separated on column chromatography using *n*-hexane and acetone as eluent. The first fraction (87–85% *n*-hexane) gave an additional amount of **3** (0.85 g) (total yield 1.35 g, 79%). The second fraction (85–80% *n*-hexane) afforded orange yellow crystals of (*Z*)-nitrile (**4**) (0.05 g, 3%), recrystallized from acetone/*n*-hexane, mp 193–194°C (lit.[2] 170–171°C), [Found C, 70.65; H, 3.51; N, 16.39. $C_{10}H_6N_2O$ requires C, 70.58; H, 3.56; N, 16.46%], ν_{max} cm^{-1} 3220 (NH); 2212 (C≡N): 1720 (C=O); 1618 (C=C), δ_H (200 MHz, DMSO-d_6) 6.87 (d, J_{HH}=7.6 Hz, H-7); 6.94 (s, =CH); 7.02, 7.39 (2t, J_{HH}=7.6 Hz, H-5, H-6); 7.70 (d, J_{HH}=7.6 Hz, H-4); 10.87 (s, NH), *m*/*z* 170 (M^+, 100%), 142 (43), 115 (30), 99 (2), 88 (9), 75 (4), 63 (6) and 52 (6). The third fraction (75–70% *n*-hexane) yielded a colourless crystals of triphenylphosphine oxide (2.5 g, 90%), mp and mixed mp with an authentic sample.

(2,3-Dihydro-2-oxo-1*H*-indol-3-yl)acetonitrile (5). The orange solution of (*E*)-nitrile (**3**) (0.68 g, 4.0 mmol) in acetic acid (10 mL) was heated under reflux. Zinc dust (0.5 g) was added in small portions and the mixture was refluxed for about 1 h. After removal of the inorganic residue by filtration, the filtrate was concentrated followed by addition of water (10 mL) and extracted with ethyl acetate. The extract was dried over anhydrous sodium sulfate and concentrated under reduced pressure. Then, *n*-hexane was added to give colourless crystalline product **5** (0.58 g, 84%), recrystallized from ethyl acetate/*n*-hexane, mp 164–165°C, [Found C, 69.69; H, 4.75; N, 16.34. $C_{10}H_8N_2O$ requires C, 69.76; H, 4.68; N, 16.27%], ν_{max} cm^{-1} 3136 (NH); 2248 (C≡N); 1707 (C=O); 1620 (C=C), δ_H (200 MHz, $CDCl_3$+drop DMSO-d_6) 2.77 (dd, $J_{H^aH^b}$=17.0 Hz, $J_{H^aH^x}$=8.4 Hz, H^a); 3.08 (dd, $J_{H^bH^a}$=17.0 Hz, $J_{H^bH^x}$ 5.0 Hz, H^b); 3.65 (dd, $J_{H^xH^a}$=8.4 Hz, $J_{H^xH^b}$=5.0 Hz, H^x); 6.94 (d, J_{HH}=7.6 Hz, H-7); 7.05, 7.27 (2t, J_{HH}=7.6 Hz, H-5, H-6); 7.43 (d, J_{HH}=7.8 Hz, H-4); 10.09 (s, NH), δ_C (67.5 MHz, DMSO-d_6) 17.6 (CH_2); 41.3 (C-3); 109.6 (C-7); 118.3 (CN); 121.7 (C-5); 124.3 (C-4); 127.2 (C-3a); 128.7 (C-6); 142.8 (C-7a); 176.5 (C=O), *m*/*z* 172 (M^+, 69%), 146 (3), 132 (100), 117 (14), 104 (16), 89 (10), 77 (11), 63 (7) and 51 (10).

(2,3-Dihydro-1,3-dimethyl-2-oxo-1*H*-indol-3-yl)acetonitrile (6). To a solution of compound **5** (0.69 g, 4.0 mmol) in dry acetone (20 mL), anhydrous potassium carbonate (3 g) was added. The mixture was heated under reflux. Then, freshly distilled methyl iodide (4 mL) was added with continuous heating for 6 h. After removal of the inorganic residue, the solution was evaporated under reduced pressure to give an oily product **6** (0.66 g, 83%), purified by column chromatography using 10% acetone/*n*-hexane as eluent. [Found C, 71.91; H, 6.10; N, 14.04. $C_{12}H_{12}N_2O$ requires C, 71.98; H, 6.04; N, 13.99%], ν_{max} cm^{-1} (thin film): 2249 (C≡N); 1714 (C=O). 1614 (C=C), δ_H (270 MHz, $CDCl_3$) 1.45 (s, Me at C-3); 2.50, 2.78 (2d, $J_{H^aH^b}$=16.8 Hz, H^a, H^b); 3.17 (s, *N*-Me); 6.84 (d, J_{HH}=7.6 Hz, H-7); 7.06, 7.29 (2t, J_{HH}=7.8 Hz, H-5, H-6); 7.40 (d, J_{HH}=7.3 Hz, H-4), δ_C (67.5 MHz, $CDCl_3$) 22.0 (Me at C-3); 26.1 (CH_2); 26.3 (*N*-Me); 44.7 (C-3); 108.6 (C-7); 116.5 (CN); 122.9 (C-5); 123.1 (C-4); 129.0 (C-6); 130.8 (C-3a); 142.5 (C-7a); 177.3 (C=O), *m*/*z* 200 (M^+, 57%), 194 (7), 160 (100), 145 (4), 130 (9), 117 (9), 115 (4), 89 (3), 77 (3) and 51 (2).

Reaction of (*E*)-nitrile (3) with trimethyl phosphite (7a). To a suspension of compound **3** (1.40 g, 8.0 mmol) in dry benzene (30 mL), freshly distilled trimethyl phosphite (**7a**) (4 mL) was added. The mixture was heated under reflux at 70°C for about 10 h. Then, the solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel with *n*-hexane and acetone (increasing amounts) as eluent to give four fractions. The first fraction (65–60% *n*-hexane) afforded a small amount of colourless crystalline product of dimethyl [cyano(2,3-dihydro-2-oxo-1H-indol-3-yl)methyl]phosphonate (isomer $\mathbf{8a_A}$), examined by ^1H NMR spectrum, mp 164–165°C, [Found C, 51.35; H, 4.59; N, 10.08; P, 11.12. $C_{12}H_{13}N_2O_4P$ requires C, 51.43; H, 4.68; N, 10.00; P, 11.05%], ν_{max} cm^{-1} 3209 (NH); 2241 (C≡N): 1724 (C=O); 1622 (C=C); 1240 (P=O); 1028 (P-O-Me), δ_H (200 MHz, DMSO-d_6) 3.51, 3.68 [2d, J_{HP}=11.2 Hz, $P(OMe)_2$]; 4.17 (dd, J_{HP}=25.4 Hz, J_{HH}=3.4 Hz, H-3); 4.49 (dd, J_{HP}=23.6 Hz, J_{HH}=3.4 Hz, H-8); 6.89 (d, J_{HH}=7.6 Hz, H-7); 7.04, 7.27 (2t, J_{HH}=7.6 Hz, H-5, H-6); 7.49 (d, J_{HH}=7.6 Hz, H-4); 10.67 (s, NH), δ_C (67.5 MHz, DMSO-d_6) 28.9 (d, $^1J_{PC}$=141.6 Hz, C-8); 43.1 (C-3); 53.4, 53.8 [2d, $^2J_{PC}$=7.4 Hz, $P(OMe)_2$]; 109.7 (C-7); 116.1 (d, $^2J_{PC}$=8.6 Hz, C≡N); 121.4 (C-5); 124.7 (C-4); 125.5 (d, $^3J_{PC}$=8.5 Hz, C-3a); 128.8 (C-6); 142.97 (C-7a); 175.2 (d, $^3J_{PC}$=14.6 Hz, C=O), *m*/*z* 280 (M^+, 100%), 252 (3), 233 (2), 185 (2), 170 (91), 154 (13), 145 (50), 132 (29), 110 (90), 95 (10), 80 (20), 77 (12) and 51 (5). The second fraction contained a mixture of the two isomers $\mathbf{8a_A}$ and $\mathbf{8a_B}$ (0.43 g, 23%). The isomer $\mathbf{8a_B}$ could not be isolated by either column chromatography or fractional crystallization. The ^1H NMR and ^{13}C NMR spectra of $\mathbf{8a_B}$ were taken from the isomeric mixture, δ_H (200 MHz, DMSO-d_6) 3.81, 3.84 [2d, J_{HP}=11.2 Hz, $P(OMe)_2$]; 4.05 (dd, J_{HP}=16.6 Hz, J_{HH}=2.4 Hz, H-3); 4.43 (dd, J_{HP}=24.6 Hz, J_{HH}=2.6 Hz, H-8); 6.91 (d, J_{HH}=7.6 Hz, H-7); 7.04, 7.29 (2t, J_{HH}=7.6 Hz, H-5, H-6); 7.59 (d, J_{HH}=7.6 Hz, H-4); 10.80 (s, NH), δ_C (67.5 MHz, DMSO-d_6) 29.2 (d, $^1J_{PC}$=145.3 Hz, C-8); 43.0 (C-3); 53.1, 54.4 [2d, $^2J_{PC}$=7.4 Hz, $P(OMe)_2$]; 109.7 (C-7); 114.4 (d, $^2J_{PC}$=7.3 Hz, C≡N); 121.6 (C-5); 124.6 (C-3a); 125.9 (C-4); 129.0 (C-6); 143.0 (C-7a); 174.3 (C=O). The third fraction (40–35% *n*-hexane gave colourless crystals of the dimeric structure $\mathbf{9a_A}$ (0.23 g, 12%), recrystallized from acetone/*n*-hexane, mp 263-264°C, [Found C, 58.63; H, 4.28; N, 12.50; P, 6.93. $C_{22}H_{19}N_4O_5P$ requires C, 58.67; H, 4.25; N, 12.44; P, 6.88%], ν_{max} cm^{-1} 3419, 3318 (NH_2); 3185 (NH); 2254 (C≡N); 1730, 1702 (C=O); 1635 (C=C); 1213 (P=O);

1057, 1018 (P-O-Me), δ_{H} (200 MHz, DMSO-d_6) 3.26, 3.43 [2d, J_{HP}=11.2 Hz, P(OMe)$_2$]; 3.94 (s, H-8); 6.27 (s, NH$_2$); 6.88, 6.97 (2d, J_{HH}=7.8 Hz, H-7, H-7′); 7.09, 7.12 (2t, J_{HH}=7.6 Hz, H-5, H-5′); 7.26 (d, J_{HH}=7.2 Hz, H-4); 7.28, 7.35 (2t, J_{HH}=7.8 Hz, H-6, H-6′); 8.21 (d, J_{HH}=7.6 Hz, H-4′); 10.69, 11.03 (2s, 2NH), δ_{C} (67.5 MHz, DMSO-d_6) 45.2 (d, $^3J_{\mathrm{PC}}$=13.4 Hz, C-8); 51.3, 51.9 [2d, $^2J_{\mathrm{PC}}$=4.9 Hz, P(OMe)$_2$]; 61.4 (d, $^3J_{\mathrm{PC}}$=14.6 Hz, C-3′); 63.6 (d, $^2J_{\mathrm{PC}}$=17.1 Hz, C-3); 86.1 (d, $^1J_{\mathrm{PC}}$=199.0 Hz, C-10); 109.7, 110.4 (C-7, C-7′); 116.0 (C≡N); 122.1, 122.3 (C-5, C-5′); 124.0, 126.8 (C-4, C-4′); 127.0, 129.3 (C-3a, C-3′a); 129.9, 130.9 (C-6, C-6′); 141.8, 142.9 (C-7a, C-7′a); 163.1 (d, $^2J_{\mathrm{PC}}$=17.1 Hz, C-9); 176.0, 177.8 (2 C═O), *m/z* 450 (M$^+$, 100%), 422 (15), 358 (3), 355 (8), 341 (69); 313 (15), 296 (9); 270 (3), 142 (4), 110 (5) and 79 (2). The fourth fraction (35–30% *n*-hexane) yielded colourless crystalline isomer **9a$_{\mathbf{B}}$** (0.55 g, 29%), recrystallized from acetone/*n*-hexane, mp 249–250°C, [Found C, 58.73; H, 4.18; N, 12.39; P, 6.95. $C_{22}H_{19}N_4O_5P$ requires C, 58.67; H, 4.25; N, 12.44; P, 6.88%], $\nu_{\max}$ cm^{-1} 3411, 3316 (NH$_2$); 3240 (NH); 1726 (C═O); 1620 (C═C); 1213 (P═O); 1026 (P-O-Me), δ_{H} (200 MHz, DMSO-d_6) 3.16, 3.46 [2d, J_{HP}=11.2 Hz, P(OMe)$_2$]; 4.27 (s, H-8); 6.32 (s, NH$_2$); 6.89, 7.01 (2d, J_{HH}=7.6 Hz, H-7, H-7′); 7.12, 7.20 (2t, J_{HH}=7.8 Hz, H-5, H-5′); 7.30, 7.40 (2t, J_{HH}=7.8 Hz, H-6, H-6′); 7.56, 7.62 (2d, J_{HH}=7.2 Hz, H-4, H-4′); 10.69, 11.01 (2s, 2NH), δ_{C} (67.5 MHz, DMSO-d_6) 45.3 (d, $^3J_{\mathrm{PC}}$=14.7 Hz, C-8); 51.5, 51.6 [2d, $^2J_{\mathrm{PC}}$=4.9 Hz, P(OMe)$_2$]; 61.3 (d, $^3J_{\mathrm{PC}}$=14.6 Hz, C-3′); 64.0 (d, $^2J_{\mathrm{PC}}$=17.1 Hz, C-3); 87.1 (d, $^1J_{\mathrm{PC}}$=195.3 Hz, C-10); 109.8, 110.7 (C-7, C-7′); 115.5 (C≡N); 121.7, 122.4 (C-5, C-5′); 125.1, 125.6 (C-4, C-4′); 126.9, 129.3 (C-3a, C-3′a); 129.6, 130.2 (C-6, C-6′); 142.0, 143.1 (C-7a, C-7′a); 162.1 (d, $^2J_{\mathrm{PC}}$=17.1 Hz, C-9); 175.8, 178.5 (2C═O), *m/z* 450 (M$^+$, 26%), 422 (11), 408 (4), 390 (3), 355 (23), 341 (100), 296 (22), 270 (11), 247 (4), 203 (2), 184 (4), 170 (28), 142 (28), 109 (72), 79 (31) and 77 (4).

Reaction of (*E*)-nitrile (3) with triethyl phosphite (7b). Carrying out the same experimental procedure as described above gave also four fractions. The first fraction [70–65% petroleum ether (bp 60–80°C)] afforded a small amount of colourless crystals of diethyl [cyano(2,3-dihydro-2-oxo-1*H*-indol-3-yl)methyl]phosphonate (isomer **8b$_{\mathbf{A}}$**), examined by ^{1}H NMR spectrum, mp 154–155°C, [Found C, 54.62; H, 5.51; N, 9.02; P, 10.11. $C_{14}H_{17}N_2O_4P$ requires C, 54.54; H, 5.56; N, 9.09; P, 10.05%], $\nu_{\max}$ cm^{-1} 3192 (NH); 2239 (C≡N); 1724 (C═O); 1620 (C═C): 1280 (P═O); 1014 (P-O-Et), δ_{H} (200 MHz, DMSO-d_6) 1.13, 1.19 [2t, J_{HH}=7.0 Hz, P(OCH$_2$*Me*)$_2$]; 3.69–4.08 [m, P(O*CH$_2$*Me)$_2$]; 4.16 (dd, J_{HP}=27.0 Hz, J_{HH}=3.4 Hz, H-3); 4.36 (dd, J_{HP}=23.4 Hz, J_{HH}=3.4 Hz, H-8); 6.87 (d, J_{HH}=7.6 Hz, H-7); 7.02, 7.26 (2t, J_{HH}=7.6 Hz, H-5, H-6); 7.47 (d, J_{HH}=7.8 Hz, H-4); 10.63 (s, NH), δ_{C} (67.5 MHz, DMSO-d_6) 15.9, 16.0 [2d, $^3J_{\mathrm{PC}}$=7.4, 6.1 Hz, P(OCH$_2$*Me*)$_2$]; 29.2 (d, $^1J_{\mathrm{PC}}$=141.6 Hz, C-8); 43.1 (C-3); 63.0, 63.2 [2d, $^2J_{\mathrm{PC}}$=7.4, 6.1 Hz, P(O*CH$_2$*Me)$_2$]; 109.6 (C-7); 116.4 (d, $^2J_{\mathrm{PC}}$=7.3 Hz, C≡N); 121.3 (C-5); 124.7 (C-4); 125.5 (C-3a); 128.7 (C-6); 143.0 (C-7a); 175.3 (d, $^3J_{\mathrm{PC}}$=14.6 Hz, C═O), *m/z* 308 (M$^+$, 100%), 263 (11), 208 (5), 199 (3), 171 (74), 170 (45), 138 (63), 111 (77), 82 (47), 81 (39), 77 (33) and 65 (17). The second fraction contained a mixture of the two isomers **8b$_{\mathbf{A}}$** and **8b$_{\mathbf{B}}$** (20%). The other isomer **8b$_{\mathbf{B}}$** could not be isolated in the pure form. The ^{1}H and ^{13}C NMR spectra of **8b$_{\mathbf{B}}$** were taken from the isomeric mixture. δ_{H} (200 MHz, DMSO-d_6) 1.29 [t, J_{HH}=7.2 Hz, P(OCH$_2$*Me*)$_2$]; 3.60–4.50 [m, {P(O*CH$_2$*Me)$_2$, H-3 and H-8}]; 6.90 (d, J_{HH}=7.4 Hz, H-7); 7.02, 7.26 (2t, J_{HH}=7.4 Hz, H-5, H-6); 7.62 (d, J_{HH}=7.4 Hz, H-4); 10.77 (s, NH), δ_{C} (67.5 MHz, DMSO-d_6) 15.9, 16.0 [2d, $^3J_{\mathrm{PC}}$=7.4, 6.1 Hz, P(OCH$_2$*Me*)$_2$]; 29.9 (d, $^1J_{\mathrm{PC}}$=145.3 Hz, C-8); 43.1 (C-3); 63.7, 63.9 [2d, $^2J_{\mathrm{PC}}$=7.4, 8.9 Hz, P(O*CH$_2$*Me)$_2$]. 109.7 (C-7); 114.5 (d, $^2J_{\mathrm{PC}}$=7.3 Hz, C≡N); 121.6 (C-5); 125.4 (C-3a); 126.0 (C-4); 129.0 (C-6); 143.0 (C-7a); 174.3 (C═O). The third fraction (40–35% petroleum ether) afforded colourless crystals of isomer **9b$_{\mathbf{A}}$** (13%), recrystallized from acetone/*n*-hexane, mp 293–294°C, [Found C, 60.29; H, 4.79; N, 11.76; P, 6.51. $C_{24}H_{23}N_4O_5P$ requires C, 60.25; H, 4.85; N, 11.71; P, 6.47%], $\nu_{\max}$ cm^{-1}: 3417, 3323 (NH$_2$); 3240 (NH); 2245 (C≡N, very weak); 1728 (C═O); 1635 (C═C); 1200 (P═O); 1024 (P-O-Et), δ_{H} (200 MHz, DMSO-d_6) 0.93, 1.12 [2t, J_{HH}=7.0 Hz, P(OCH$_2$*Me*)$_2$]; 3.57–3.82 [m, P(O*CH$_2$*Me)$_2$]; 3.94 (s, H-8); 6.23 (s, NH$_2$); 6.88, 6.98 (2d, J_{HH}=7.6 Hz, H-7, H-7′); 7.09-7.13 (2t, J_{HH}=7.8 Hz, H-5, H-5′); 7.26 (d, J_{HH}=7.4 Hz, H-4); 7.28, 7.36 (2t, J_{HH}=7.8 Hz, H-6, H-6′); 8.22 (d, J_{HH}=7.8 Hz, H-4′); 10.69, 11.04 (2s, 2NH), δ_{C} (67.5 MHz, DMSO-d_6) 15.6, 15.8 [2d, $^3J_{\mathrm{PC}}$=7.3 Hz, P(OCH$_2$*Me*)$_2$]; 45.2 (d, $^3J_{\mathrm{PC}}$=14.6 Hz, C-8); 60.3, 61.0 [2d, $^2J_{\mathrm{PC}}$=4.9 Hz, P(O*CH$_2$*Me)$_2$]; 61.5 (d, $^3J_{\mathrm{PC}}$=14.6 Hz, C-3′); 63.5 (d, $^2J_{\mathrm{PC}}$=18.3 Hz, C-3); 87.4 (d, $^1J_{\mathrm{PC}}$=197.8 Hz, C-10); 109.6, 110.3 (C-7, C-7′); 116.0 (C≡N); 122.0, 122.2 (C-5, C-5′); 124.2, 126.8 (C-4, C-4′); 127.0, 129.2 (C-3a, C-3′a); 129.8, 130,8 (C-6, C-6′); 142.0, 142.9 (C-7a, C-7′a); 162.5 (d, $^2J_{\mathrm{PC}}$=15.9 Hz, C-9); 176.0, 177.8 (2 C═O), *m/z* 478 (M$^+$, 95%), 450 (10), 405 (2), 376 (4), 341 (100), 314 (17), 233 (3), 171 (7), 111 (3) and 82 (2). The fourth fraction (35–25% petroleum ether) yielded colourless crystalline product of the dimeric structure, isomer **9b$_{\mathbf{B}}$** (33%), recrystallized from acetone/*n*-hexane, mp 279–280°C, [Found C, 60.31; H, 4.76; N, 11.79; P, 6.50. $C_{24}H_{23}N_4O_5P$ requires C, 60.25; H, 4.85; N, 11.71; P, 6.47%], $\nu_{\max}$ cm^{-1} 3423, 3320 (NH$_2$); 3253 (NH); 1737, 1706 (C═O); 1624 (C═C); 1190 (P═O); 1026 (P-O-Et), δ_{H} (200 MHz, DMSO-d_6), 0,82, 1.16 [2t, J_{HH}=7.2 Hz, 6H, P(OCH$_2$*Me*)$_2$]; 3.38–3.87 [m, 4H, P(O*CH$_2$*Me)$_2$]; 4.27 (s, H-8); 6.28 (s, NH$_2$); 6.88, 7.00 (2d, J_{HH}=7.6 Hz, H-7, H-7′); 7.11, 7.20 (2t, J_{HH}=7.6 Hz, H-5, H-5′); 7.29, 7.39 (2t, J_{HH}=7.6 Hz, H-6, H-6′); 7.52, 7.59 (2d, J_{HH}=7.6 Hz, H-4, H-4′); 10.67, 10.99 (2s, 2NH), δ_{C} (67.5 MHz, DMSO-d_6) 15.6, 15.8 [2d, $^3J_{\mathrm{PC}}$=7.4 Hz, P(OCH$_2$*Me*)$_2$]; 45.3 (d, $^3J_{\mathrm{PC}}$=14.7 Hz, C-8); 60.3, 60.9 [2d, $^2J_{\mathrm{PC}}$=4.9 Hz, P(O*CH$_2$*Me)$_2$]; 61.4 (d, $^3J_{\mathrm{PC}}$=14.7 Hz, C-3′); 64.0 (d, $^2J_{\mathrm{PC}}$=17.1 Hz, C-3); 88.1 (d, $^1J_{\mathrm{PC}}$=195.3 Hz, C-10); 109.7, 110.7 (C-7, C-7′); 115.6 (C≡N); 121.6, 122.3 (C-5, C-5′); 125.0, 125.7 (C-4, C-4′); 127.0, 129.1 (C-3a, C-3′a); 129.1, 130.1 (C-6, C-6′); 142.1, 143.0 (C-7a, C-7′a); 161.6 (d, $^2J_{\mathrm{PC}}$=15.8 Hz, C-9); 175.8, 178.5 (2 C═O), *m/z* 478 (M$^+$, 40%), 450 (10), 376 (8), 369 (15), 341 (100), 296 (26), 233 (9), 229 (3), 199 (2), 170 (24), 142 (15), 115 (12), 82 (6) and 69 (12).

Reaction of methyl iodide with 9a$_{\mathbf{B}}$. A mixture of **9a$_{\mathbf{B}}$**(0.23 g, 0.5 mmol), freshly distilled methyl iodide (1.5 mL) and anhydrous powdered potassium carbonate (1 g) in dry acetone (15 mL) was gently heated, under reflux for about 5 h. After removal of the inorganic residue and volatile materials, the solid product (0.20 g, 83%) was crystallized from acetone–diethyl ether to give **10a** as colourless crystals, mp 259–260°C, [Found C, 60.31; H, 4.78; N, 11.66; P, 6.54. $C_{24}H_{23}N_4O_5P$ requires C, 60.25; H, 4.85; N, 11.71; P, 6.47%], ν_{max} cm^{-1} 3462, 3315 (NH_2); 2245 (C≡N, very weak); 1736, 1707 (C═O); 1628 (C═C); 1240 (P═O); 1012 (P-O-Me), δ_H (270 MHz, DMSO-d_6) 3.17, 3.43 [2d, J_{HP}=11.6 Hz, P(OMe)$_2$]; 3.20, 3.23 (2s, 2*N*-Me); 4.31 (s, H-8); 6.34 (s, NH_2); 7.09, 7.20 (2d, J_{HH}=7.8 Hz, H-7, H-7′); 7.21, 7.29 (2t, J_{HH}=7.4 Hz, H-5, H-5′); 7.41, 7.50 (2t, J_{HH}=7.6 Hz, H-6, H-6′); 7.62, 7.68 (2d, J_{HH}=7.3 Hz, H-4, H-4′), δ_C (67.5 MHz, DMSO-d_6) 26.7, 27.0 (2 *N*-Me); 44.7 (d, $^3J_{PC}$=14.6 Hz, C-8); 51.4, 51.9 [2d, $^2J_{PC}$=3.7 Hz, P(OMe)$_2$]; 60.9 (d, $^3J_{PC}$=13.4 Hz, C-3′); 63.5 (d, $^2J_{PC}$=17.1 Hz, C-3); 87.1 (d, $^1J_{PC}$=196.5 Hz, C-10); 108.7, 109.7 (C-7, C-7′); 115.6 (C≡N); 122.3, 122.9 (C-5, C-5′); 124.6, 125.4 (C-4, C-4′); 126.4, 128.8 (C-3a, C-3′a); 129.4, 130.2 (C-6, C-6′); 143.5, 144.6 (C-7a, C-7′a); 161.8 (d, $^2J_{PC}$=15.9 Hz, C-9); 174.0, 176.9 (2 C═O). *m/z* 478 (M$^+$, 100%), 450 (5), 383 (6), 369 (96), 341 (26), 324 (40), 294 (84), 261 (9), 247 (5), 194 (3), 184 (61), 155 (27), 130 (10) and 79 (3).

Similarly, compound **10b** was obtained as colourless crystals from the reaction of **9b$_B$** with methyl iodide under the same experimental conditions described above.

Compound 10b (88%), crystallized from chloroform–petroleum ether (bp 60–80°C), mp 256–257°C, [Found C, 61.71; H, 5.45; N, 11.01; P, 6.08. $C_{26}H_{27}N_4O_5P$ requires C, 61.66; H, 5.37; N, 11.06; P, 6.12%], ν_{max} cm^{-1} 3411, 3313 (NH_2); 2240 (C≡N, very weak); 1728 (C═O); 1635, 1612 (C═C); 1209 (P═O); 1049, 1018 (P-O-Et), δ_H (270 MHz, $CDCl_3$) 0.75, 1.20 [2t, J_{HH}=7.0 Hz, P(OCH$_2$*Me*)$_2$]; 3.21, 3.23 (2s, 2 *N*-Me); 3.35–4.10 [m, P(O*CH*$_2$Me)$_2$]; 4.46 (s, H-8); 5.16 (s, NH_2); 6.84, 6.92 (2d, J_{HH}=7.6 Hz, H-7, H-7′); 7.15, 7.21 (2t, J_{HH}=7.4 Hz, H-5, H-5′), 7.32, 7.40 (2t, J_{HH}=7.8 Hz, H-6, H-6′); 7.49, 7.59 (2d, J_{HH}=7.6 Hz, H-4, H-4′), δ_C (67.5 MHz, $CDCl_3$) 15.5, 15.8 [2d, $^3J_{PC}$=7.4 Hz, P(OCH$_2$*Me*)$_2$; 26.7, 27.1 (2 *N*-Me); 44.5 (d, $^3J_{PC}$=13.5 Hz, C-8); 60.9, 62.0 [2d, $^2J_{PC}$=4.9 Hz, P(O*CH*$_2$Me)$_2$]; 61.3 (d, $^3J_{PC}$=14.7 Hz, C-3′); 63.9 (d, $^2J_{PC}$=18.3 Hz, C-3); 91.3 (d, $^1J_{PC}$=192.8 Hz, C-10); 108.3, 109.2 (C-7, C-7′); 115.4 (C≡N); 122.5, 123.5 (C-5, C-5′); 125.1, 125.3 (C-4, C-4′); 125.4, 128.9 (C-3a, C-3′a); 129.5, 130.6 (C-6, C-6′); 143.6, 143.9 (C-7a, C-7′a); 160.6 (d, $^2J_{PC}$=15.8 Hz, C-9); 174.3, 176.5 (2 C═O), *m/s* 506 (M$^+$, 100%), 478 (4), 404 (3), 397 (13), 369 (85), 324 (26), 322 (44), 310 (13), 265 (4), 247 (16), 225 (3), 184 (36), 155 (25), 138 (11) and 111 (6).

Reaction of (*E*)-nitrile (3) with dimethyl phosphite (11a). A mixture of compound **3** (2.55 g, 15 mmol) and freshly distilled dimethyl phosphite (**11a**) (4 mL) was heated without solvent at 100–105°C. After 30 h, the excess dimethyl phosphite was removed under reduced pressure and the oily residue was chromatographed on silica gel, using acetone and *n*-hexane as eluent to give two fractions. The first fraction (65–60% *n*-hexane) yielded colourless crystalline product (1.31 g, 36%), proved to be the phosphonate **8a** containing a mixture of the two isomers **8a$_A$** and **8a$_B$** examined by its ^{1}H NMR spectrum. The second fraction (40–35% *n*-hexane) gave a colourless crystalline product (1.12 g, 31%) proved to be **9a$_B$** (mp, mixed mp and ^{1}H NMR spectrum compared with an authentic sample previously reported).

Similarly, compounds **8b** (as a mixture of the two isomers **8b$_A$**, **8b$_B$**) and isomer **9b$_B$** were formed from the reaction of **3** with diethyl phosphite (**11b**) under the same experimental conditions described above. The first fraction yielded a colourless crystals of the phosphonate **8b** (34%) as a mixture of the two isomers **8b$_A$** and **8b$_B$** (shown by its ^{1}H NMR spectrum). The second fraction afforded a colourless crystals of the isomer **9b$_B$** (25%) (identified by its mp, mixed mp and comparative ^{1}H NMR spectrum with an authentic sample previously reported).

Reaction of methyl iodide with the phosphonate 8b as a mixture of the two isomers 8b$_A$ and 8b$_B$. To a solution of the mixture **8b** (0.93 g, 3 mmol) in dry acetone (30 mL), anhydrous potassium carbonate (2 g) and freshly distilled methyl iodide (4 mL) were added. The mixture was gently heated under reflux for about 8 h. Then, the inorganic residue and volatile materials were removed and the residual substance was chromatographed on silica gel using *n*-hexane and acetone as eluent to give two fractions. The first fraction (80–75% *n*-hexane) gave colourless crystals of diethyl [1-cyano-1-(2,3-dihydro-1,3-dimethyl-2-oxo-1H-indol-3-yl)ethyl]phosphonate (**16a**) (0.34 g, 33%), recrystallized from benzene/*n*-hexane, mp 89–90°C, [Found 58.23; H, 6.59; N, 8.04; P 8.79. $C_{17}H_{23}N_2O_4P$ requires C, 58.28; H, 6.62; N, 8.00; P, 8.84%], ν_{max} cm^{-1} 2237 (C≡N); 1711 (C═O); 1612 (C═C); 1261 (P═O); 1049 (P-O-Et), δ_H (200 MHz, $CDCl_3$) 1.05, 1.18 [2t, J_{HH}=7.2 Hz, P(OCH$_2$*Me*)$_2$]; 1.62 (s, Me at C-3); 1.95 (d, J_{HP}=15.4 Hz, Me at C-8); 3.19 (s, *N*-Me); 3.39–4.15 [m, P(O*CH*$_2$Me)$_2$]; 6.83 (d, J_{HH}= 7.6 Hz, H-7); 7.07, 7.31 (2t, J_{HH}=7.6 Hz, H-5, H-6); 7.72 (d, J_{HH}=7.4 Hz, H-4), δ_C (67.5 MHz, $CDCl_3$) 16.0 (d, $^2J_{PC}$=6.1 Hz, Me at C-8); 16.1, 16.4 [2d, $^3J_{PC}$=4.9, 3.6 Hz, P(OCH$_2$*Me*)$_2$]; 21.3 (d, $^3J_{PC}$=9.8 Hz, Me at C-3); 26.3 (*N*-Me); 43.1 (d, $^1J_{PC}$=144.1 Hz, C-8); 47.0 (C-3); 63.7, 63.8 [2d, $^2J_{PC}$=7.3, 8.5 Hz, P(O*CH*$_2$Me)$_2$]; 108.0 (C-7); 118.8 (d, $^2J_{PC}$=8.5 Hz, C≡N); 122.3 (C-5); 124.6 (C-4); 128.8 (C-6); 130.7 (C-3a); 142.2 (C-7a); 175.7 (C═O), *m/z* 350 (M$^+$, 36%), 305 (1), 249 (1), 213 (1), 191 (2), 160 (100) and 132 (3). The second fraction (75–72% *n*-hexane) afforded colourless crystals of diethyl [cyano(2,3-dihydro-1,3-dimethyl-2-oxo-1H-indol-3-yl)methyl]phosphonate (**16b**) (0.39 g, 38%), recrystallized from benzene/*n*-hexane, mp 132–133°C, [Found C, 57.20; H, 6.33; N, 8.27; P, 9.28, $C_{16}H_{21}N_2O_4P$ requires C, 57.14; H, 6.29; N, 8.33; P, 9.21%]. ν_{max} cm^{-1} 2241 (C≡N); 1709 (C═O); 1614 (C═C); 1265 (P═O); 1020 (P-O-Et), δ_H (200 MHz, $CDCl_3$) 1.02, 1.23 [2t, J_{HH}=7.2 Hz, P(OCH$_2$*Me*)$_2$]; 1.57 (d, $^4J_{HP}$=2.0 Hz, Me at C-3); 3.22 (s, *N*-Me); 3.23–4.09 (m, P(O*CH*$_2$Me)$_2$]; 3.64 (d overlaped, $^2J_{HP}$=23.0 Hz, H-8); 6.88 (d, J_{HH}=7.8 Hz, H-7); 7.09, 7.33 (2t, J_{HH}=7.6 Hz, H-5, H-6); 7.58 (d, J_{HH}=7.6 Hz, H-4), δ_C (67.5 MHz, $CDCl_3$) 15.9, 16.0 [2d, $^3J_{PC}$=2.4 Hz, P(OCH$_2$*Me*)$_2$]; 24.6 (d, $^3J_{PC}$=13.5 Hz, Me at C-3); 26.6 (*N*-Me); 37.2 (d, $^1J_{PC}$=141.6 Hz, C-8); 45.8 (d, $^2J_{PC}$=2.4 Hz, C-3); 63.2, 63.4 [2d, $^2J_{PC}$=7.3, 6.1 Hz, P(O*CH*$_2$Me)$_2$]; 108.5 (C-7); 115.0 (d, $^2J_{PC}$=9.8 Hz, C≡N); 122.4 (C-5); 123.9 (C-4); 129.1 (C-6); 129.4 (C-3a); 143.3 (C-7a); 176.6 (C═O), *m/z* 336 (M$^+$, 36%), 183 (3), 160 (100) and 130 (4).

Preparation of 3-dicyanomethylene-2-oxindole. A mixture of isatin (**1**) (1.47 g, 10 mmol) and malononitrile (0.73 g, 11 mmol) in absolute ethanol (30 mL) was stirred at room temperature for about 15 min. During this time, the isatin dissolved and a deep red precipitate was formed. It was filtered off and crystallized from absolute ethanol to give 1.71 g of 3-dicyanomethylene-2-oxindole, mp 237–238°C (lit.[15] 235°C). The filtrate afforded upon concentration an additional amount of 0.14 g (total yield 1.85 g, 95%), $\nu_{\max}$ cm^{-1} 3261 (NH); 2240 (C≡N, very weak); 1730, 1716 (C=O); 1620, 1585 (C=C).

Preparation of dimethyl [dicyano(2,3-dihydro-2-oxo-1*H*-indol-3-yl)methyl]phosphonate (17a). A mixture of 3-dicyanomethylene-2-oxindole (3.0 g, 15.4 mmol) and freshly distilled dimethyl phosphite (3 mL) was heated under reflux at 100–105°C. After about 2 h, the reaction mixture was allowed to stand overnight. The colourless crystals, thus formed, was filtered off and washed with dry ether. Recrystallization from ethyl methyl ketone afforded the phosphonate **17a** (3.2 g, 66%), mp 226–227°C (lit.[9] 222°C), [Found C, 51.24; H, 3.90; N, 13.74; P, 10.21. $C_{13}H_{12}N_3O_4P$ requires C, 51.15; H, 3.96; N, 13.77; P, 10.15%], $\nu_{\max}$ cm^{-1} 3151 (NH); 1724 (C=O, amide); 1255 (P=O); 1026 (P-O-Me), δ_H (200 MHz, $CDCl_3$+DMSO-d_6) 3.66, 3.69 [2d, J_{HP}=11.0 Hz, P(OMe)$_2$]; 4.81 (d, J_{HP}=6.8 Hz, H-3); 6.88 (d, J_{HH}=8.0 Hz, H-7); 7.00, 7.25 (2t, J_{HH}=7.8 Hz, H-5, H-6); 7.53 (d, J_{HH}=7.8 Hz, H-4); 10.90 (s, NH), δ_C (67.5 MHz, DMSO-d_6) 27.0 (C-3); 52.9 (d, $^1J_{PC}$=139.2 Hz, C-8); 55.5, 57.7 [2d, $^2J_{PC}$=7.3 Hz, P(OMe)$_2$]; 110.9 (C-7); 111.1, 111.5 (2d, $^2J_{PC}$=14.6, 8.6 Hz, 2 C≡N); 121.4 (d, $^3J_{PC}$=5.1 Hz, C-3a); 122.8 (d, $^5J_{PC}$=2.5 Hz, C-5); 125.8 (d, $^4J_{PC}$=2.4 Hz, C-4); 131.2 (d, $^6J_{PC}$=2.4 Hz, C-6); 143.0 (d, $^4J_{PC}$=7.4 Hz, C-7a); 170.6 (d, $^3J_{PC}$=2.5 Hz, C=O).

Diethyl [dicyano(2,3-dihydro-2-oxo-1*H*-indol-3-yl)methyl]-phosphonate (17b) (69%) was obtained similarly from 3-dicyanomethylene-2-oxindole and diethyl phosphite, recrystallized from ethyl methyl ketone, mp 175–176°C (lit.[9] 164°C), [Found C, 53.97; H, 4.92; N, 12.55; P, 9.38. $C_{15}H_{16}N_3O_4P$ requires C, 54.06; H, 4.84; N, 12.61; P, 9.29%], $\nu_{\max}$ cm^{-1} 3124 (NH); 1726 (C=O, amide); 1248 (P=O); 1020 (P-O-Et), δ_H (200 MHz, $CDCl_3$) 1.35, 1.39 [2t overlaped, J_{HH}=7.2 Hz, P(OCH$_2$*Me*)$_2$]; 4.25 [m, P(O*CH*$_2$Me)$_2$]; 4.77 (d, J_{HP}=6.6 Hz, H-3); 6.82 (d, J_{HH}=7.8 Hz, H-7); 7.18 7.35 (2t, J_{HH}=7.6 Hz, H-5, H-6); 7.71 (d, J_{HH}=7.6 Hz, H-4); 9.00 (s, NH).

Dimethyl [dicyano(2,3-dihydro-1,3-dimethyl-2-oxo-1*H*-indol-3-yl)methyl]phosphonate (19a). To a solution of **17a** (0.31 g, 1 mmol) in dry acetone (20 mL), anhydrous potassium carbonate (2 g) was added. The mixture was gently heated at 70°C. Then, freshly distilled methyl iodide (1 mL) was added with continuous heating for about 30 min. After the reaction has been completed (examined by TLC), the inorganic and volatile materials were removed. The residual substance triturated with *n*-hexane to give colourless crystalline product of **19a** (0.25 g, 76%), recrystallized from benzene/*n*-hexane, mp 142–143°C, [Found C, 54.14; H, 4.76; N, 12.51; P, 9.35. $C_{15}H_{16}N_3O_4P$ requires C, 54.05; H, 4.84; N, 12.60; P, 9.29%], $\nu_{\max}$ cm^{-1} 1718 (C=O, amide); 1267 (P=O); 1031 (P-O-Me), δ_H (200 MHz, $CDCl_3$) 1.90 (s, Me at C-3); 3.31 (s, 3H, *N*-Me); 3.81, 3.89 [2d, J_{HH}=11.0 Hz, P(OMe)$_2$]; 6.96 (d, J_{HH}=8.0 Hz, H-7); 7.22, 7.49 (2t, J_{HH}=7.8 Hz, H-5, H-6) 7.85 (d, J_{HH}=7.6 Hz, H-4), δ_C (67.5 MHz, $CDCl_3$) 22.2 (d, $^3J_{PC}$=4.9 Hz, Me at C-3); 27.1 (*N*-Me); 35.4 (d, $^2J_{PC}$=2.9 Hz, C-3); 54.4, 56.1 [2d, $^2J_{PC}$=7.8 Hz, P(OMe)$_2$]; 55.7 (d, $^1J_{PC}$=140.4 Hz, C-8); 109.3 (C-7); 113.6, 113.9 (2d, $^2J_{PC}$=4.9, 7.8 Hz, 2 C≡N); 120.3 (d, $^3J_{PC}$=5.9 Hz, C-3a); 123.8 (C-5); 126.7 (d, $^4J_{PC}$=3.9 Hz, C-4); 131.3 (d, $^6J_{PC}$=2.0 Hz, C-6): 144.4 (d, $^4J_{PC}$=6.8 Hz, C-7a); 168.5 (C=O), *m*/*z* 333 (M$^+$, 77%), 318 (2), 254 (100), 224 (20), 198 (25), 171 (20), 146 (35), 117 (11); 109 (25), 93 (83), 79 (10) and 63 (7).

The phosphonate **19b** was also obtained as colourless crystals when **17b** reacted with methyl iodide under the same experimental conditions described above.

Diethyl [dicyano(2,3-dihydro-1,3-dimethyl-2-oxo-1*H*-indol-3-yl)methyl]phosphonate (19b) (72%), crystallized from benzene/*n*-hexane, mp 136–137°C, [Found C, 56.43; H, 5.62; N, 11.58; P, 8.65. $C_{17}H_{20}N_3O_4P$ requires C, 56.51; H, 5.58; N, 11.63; P, 8.57%], $\nu_{\max}$ cm^{-1} 1720 (C=O, amide); 1263 (P=O); 1018 (P-O-Et), δ_H (200 MHz, $CDCl_3$) 1.222, 1.689 [2dt, J_{HH}=7.0 Hz, J_{HP}=0.8 Hz, P(OCH$_2$ *Me*)$_2$]; 1.92 (s, Me at C-3); 3.29 (s, *N*-Me); 4.19 [m, P(O*CH*$_2$Me)$_2$]; 6.94 (d, J_{HH}=7.8 Hz, H-7); 7.20, 7.47 (2t, J_{HH}=7.8 Hz, H-5, H-6); 7.82 (d, J_{HH}=7.6 Hz, H-4). *m*/*z* 361 (M$^+$, 100%), 346 (4), 282 (92), 254 (6), 224 (7), 210 (25), 198 (72), 171 (11), 146 (42), 109 (7) and 58 (13).

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