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Indium triflate-catalyzed coupling of indoles with acyl phosphonates: synthesis of bis(indolyl)methane phosphonates

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ABSTRACT

The coupling reaction of *N*-methylindole with alkyl and aryl phosphonate is described. The reaction works in the presence of 10 mol % of indium triflate and furnished bis(indolyl)methane phosphonates in good yield and high selectivity.

1. Introduction

Bis(indolyl)methanes are an important class of heterocyclic compounds with diverse pharmacological activities, such as fibromyalgia, chronic fatigue, and irritable bowel syndrome.[1] They promote beneficial estrogen metabolism[2] and induce apoptosis in human cancer cells.

The development of new methods for the synthesis of bis(indolyl)methanes and their derivatives is of interest in view of their versatile biological and pharmacological properties.[1b,c] Several synthetic methods for the preparation of bis(indolyl)alkane derivatives have been reported in the literature by the reaction of indoles with various carbonyl compounds in the presence of Lewis acid[3] and protic acid.[4] Metal triflates, gallium(III) halide, and molecular iodine have also been used for the synthesis of bis(indolyl)alkanes.[5] We previously showed that the Friedel–Crafts reaction of pyrrole derivatives with α,β-unsaturated compounds catalyzed by metal triflates furnished a conjugate addition product.[5d]

Shortly thereafter, we published several papers in which acyl phosphonates were used as an acceptor. The introduction of a phosphonate moiety to a bis indole structure may show interesting biological activity and be used as precursors for the synthesis of various interesting compound. Therefore, the development of methods via the combination of two previous works for the synthesis of bis(indolyl) phosphonate can be an interesting reaction regarding the synthetic organic chemistry and biological aspects. As we described recently, acyl phosphonates are readily available from the corresponding carboxylic acids and can be used as both an electrophile and an acylanion equivalent.[6] In light of the metal triflate catalyzed addition of indole to carbonyl compounds, and based on our previous studies carried out with acyl phosphonates,[7] we report an approach for the selective reaction of indole with acyl phosphonates by using metal triflate to obtain bis(indolyl)phosphonates. To the best of our knowledge, the addition of indole to the acyl phosphonates has not been reported so far.

2. Results and discussion

In our first trial indole and benzoyl phosponate were reacted in THF in the presence of a catalytic amount of indium triflate (10%). After 6 h, no change was observed at room temperature and then the mixture was heated under reflux for 3 h. According to TLC, several spots were observed. GC–MS analysis of the reaction showed that a trace amount of the bis(indolyl)methane phosphonate (**3a**) was present in the reaction mixture, but no formation of a single addition product was observed. The same procedure was applied to *m*-chlorobenzoyl phosphonate and bis(indolyl)methane phosphonate **3b** was isolated in 9% yield. Many attempts were made to obtain the addition reaction in higher yield but without success (temperature, equivalents, reaction sequence, etc.). It is known in the literature that the amine can give various reactions including the cleavage of the C–P bond of acyl phosphonates to form amides.[8] Close inspection of the reaction showed the decomposition of phosphonates. After this result, we turned our attention to *N*-substituted indoles for avoiding C–P bond cleavage. *N*-Methylindole **2** is used as a starting material and the reaction with $In(OTf)_3$ (10 mol %) was repeated at room temperature. The purified product was obtained in 44% yield and identified as bis(indolyl)methane phosphonate **3c** as shown in Scheme 1. No mono addition product was observed by monitoring the reaction by TLC and GC–MS. Heating the reaction mixture at reflux in THF (3–6 h) and the use of 2.2 equiv of **2** increased the yield to 81% after purification (Scheme 1).

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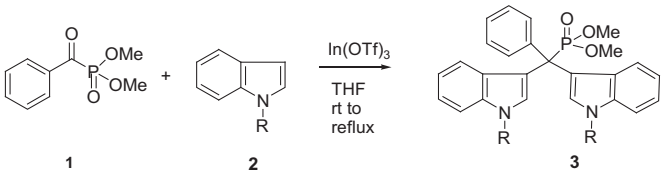


Scheme 1.

The formation reaction of **3c** was repeated with various Lewis acids and the formation of the product is monitored by TLC and GC–MS. Among the Lewis acids that were tested, such as $Bi(OTf)_3$, $Cu(OTf)_2$, $InCl_3$, $InBr_3$, InI_3, YCl_3, $Y(OTf)_3$, $Sc(OTf)_3$, and $BiCl_3$, $In(OTf)_3$ (10 mol %) was found to be the most effective for this conversion.

The scope and generality of this process are illustrated with various phosphonates. The results are shown in Table 1. Aliphatic and aromatic phosphonates underwent smooth coupling with *N*-methylindole to afford the corresponding bis(indolyl)methane phosphonates (Table 1). In the absence of a catalyst, no reaction was observed and as a solvent, THF appeared to give the best results among the other solvents used, i.e, toluene, diethylether.

In summary, we have described a simple, convenient, and efficient protocol for the synthesis of bis(indolyl)methane phosphonates from *N*-methylindoles and acyl phosphonates using 10 mol % of $In(OTf)_3$ as a catalyst. This process offers several advantages, such as good conversions, high selectivity, experimental simplicity, and high catalytic activity, which makes it a useful and attractive strategy for the preparation of bis(indolyl)methane phosphonates in a single step operation.

3. Experimental

3.1. Materials and methods

All of the reactions that were sensitive to air or moisture was conducted in flame-dried glassware under a dry Argon atmosphere. THF was distilled over sodium and benzophenone. TLC was carried out on aluminum sheets precoated with silica gel 60 F_{254} (Merck), and the spots were visualized with UV light (λ=254 nm). Column chromatography was conducted on silica gel 60 (40–63 μm). NMR spectra were recorded on a Bruker DPX 400. Chemical shifts are reported in parts per million relative to $CHCl_3$ (1H: δ=7.27), $CDCl_3$

Table 1
Bisindolylphosphonate synthesized

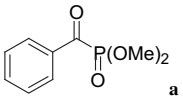
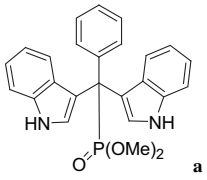
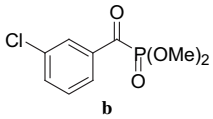
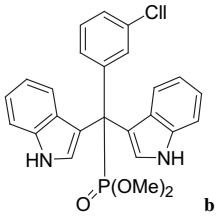
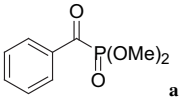
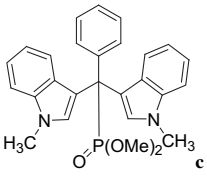
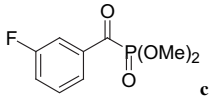
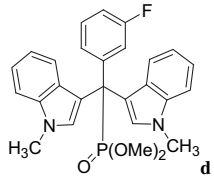
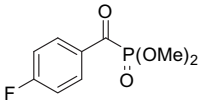
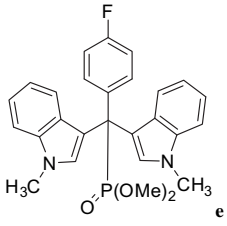
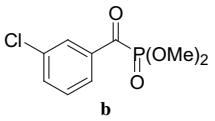
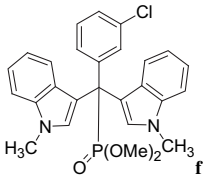
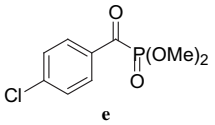
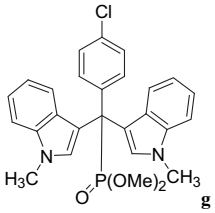
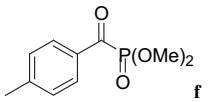
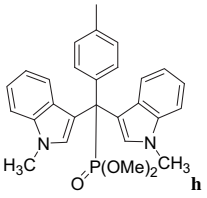
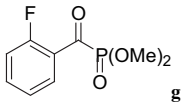
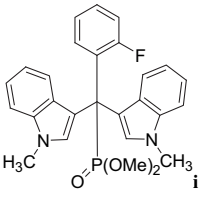
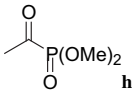
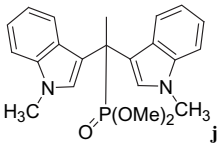
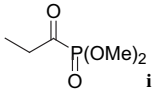
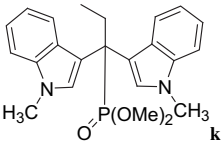
Entry	Acyl phosphonates **1**	Products **3**	Time (h)	Yield (%)
1	 **a**	 **a**	6	>5
2	 **b**	 **b**	6	9
3	 **a**	 **c**	4	81
4	 **c**	 **d**	3	80
5	 **d**	 **e**	3	77

Table 1 (*continued*)

Entry	Acyl phosphonates **1**	Products **3**	Time (h)	Yield (%)
6	 **b**	 **f**	3	74
7	 **e**	 **g**	4	81
8	 **f**	 **h**	3	78
9	 **g**	 **i**	3	68
10	 **h**	 **j**	4	77
11	 **i**	 **k**	4	71

(^{13}C: δ=77.0 ppm) and CCl_4 (^{13}C: δ=96.4 ppm). Elemental analyses: Leco CHNS 932 analyzer.

3.2. General procedure for dimethyl bis(1-methyl-indol-3-yl) (phenyl)methylphosphonate

To a solution of 10 mol % of indium triflate in THF (5 mL) at room temperature was added acyl phosphonate (1 mmol, 1 equiv) under argon, and the reaction mixture was stirred for 5 min, and then 1-methylindole (2.2 mmol, 288 mg, 2.2 equiv) was added. The resultant reaction mixture was heated at 50 °C for the time indicated in Table 1 until the disappearance of acyl phosphonate was indicated by TLC. The reaction mixture was cooled to room temperature, diluted with ether and was washed with saturated $NaHCO_3$ solution (3×10 mL). The combined organic phase was dried over $MgSO_4$, and then evaporated under reduced pressure. The crude product was purified by flash column chromatography by using EtOAc–hexane (4:1).

*3.2.1. Dimethyl bis(1-methyl-1H-indol-3-yl)(phenyl)methylphosphonate (**3c**).* Orange needles, 371 mg (81%), mp 223-222 °C; *Rf*: 0.43 (EtOAc); IR (KBr): ν=3518, 3052, 2953, 1600, 1530, 1480, 1374, 1208, 1070, 1048, 815, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J=7.5 Hz, 2H), 7.17–7.06 (m, 7H), 6.98 (t, J=7.5 Hz, 2H), 6.85 (d, J=2.3 Hz, 2H), 6.72 (t, J=7.4 Hz, 2H), 3.62 (s, 6H, $-NCH_3$), 3.37 (d, J=10.5 Hz, 6H, $-OCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.4 (d, J_{C-P}=4.4 Hz), 136.2, 129.5 (d, J_{C-P}=7.0 Hz), 129.1 (d, J_{C-P}=6.2 Hz), 126.5, 126.2 (d, J_{C-P}=6.6 Hz), 125.6, 122.1, 120.1, 117.6, 113.2 (d, J_{C-P}=6.7 Hz), 107.7, 53.5

(d, J_{C-P}=8.0 Hz, −O*C*H$_3$), 52.3 (d, J_{C-P}=138.6 Hz, −*C*PO(OCH$_3$)$_2$), 31.6 (−NC*H*$_3$). Anal. Calcd for $C_{27}H_{27}N_2O_3P$ (458.18): C, 70.73; H, 5.94; N, 6.11. Found: C, 70.52; H, 5.54; N, 5.88.

*3.2.2. Dimethyl (3-fluorophenyl)bis(1-methyl-1H-indol-3-yl) methylphosphonate (**3d**).* Violet solid, 381 mg (80%), mp 135–136 °C; R_f: 0.47 (EtOAc); IR (KBr): ν=3462, 2941, 1617, 1585, 1485, 1374, 1241, 1064, 1036, 804, 749 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, J=7.8 Hz, 1H), 7.46 (d, J=11.3 Hz, 1H), 7.26–7.09 (m, 5H), 7.12 (t, J=7.7 Hz, 2H), 7.00 (d, J=2.2 Hz, 2H), 6.93 (d, J=8.1 Hz, 1H), 6.86 (d, J=7.7 Hz, 2H), 3.70 (s, 6H, −NC*H*$_3$), 3.47 (d, J=10.5 Hz, −O*CH*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.4 (d, J_{C-F}=244.0 Hz), 143.0 (dd, J_{C-F}=6.6 and J_{C-P}=4.4 Hz), 137.3, 130.6 (d, J_{C-F}=6.7 Hz), 128.8 (d, J_{C-P}=8.2 Hz), 127.0 (d, J_{C-P}=6.7 Hz), 125. 8 (dd, J_{C-F}=6.1 Hz and J_{C-P}=2.6 Hz), 122.9, 121.2, 118.7, 117.2 (dd, J_{C-F}=23.3 Hz and J_{C-P}=6.2 Hz), 113.7, 113.5 (d, J_{C-F}=6.4 Hz), 108.9, 53.5 (d, J_{C-P}=7.7 Hz, −O*CH*$_3$), 52.1 (d, J_{C-P}=139.9 Hz, −*C*PO(OCH$_3$)$_2$), 32.8 (−NC*H*$_3$). Anal. Calcd for $C_{27}H_{26}FN_2O_3P$ (476.17): C, 68.06; H, 5.50; N, 5.88. Found: C, 68.42; H, 5.64; N, 5.68.

*3.2.3. Dimethyl (4-fluorophenyl)bis(1-methyl-1H-indol-3-yl)methylphosphonate (**3e**).* Violet solid, 366.5 mg (77%), mp 216–217 °C; R_f: 0.40 (EtOAc); IR (KBr): ν=3369, 3046, 2959, 1613, 1508, 1474, 1380, 1247, 1053, 1025, 815, 754 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71–7.67 (m, 2H), 7.26 (s, 2H), 7.16 (d, J=8.4 Hz, 2H), 7.12 (dd, J=8.0 and 1.0 Hz, 2H), 6.98 (d, J=2.4 Hz, 2H), 6.95 (t, J=8.9 Hz, 2H), 6.87 (t, J=8.0 Hz, 2H), 3.73 (s, 6H, −NC*H*$_3$), 3.48 (d, J=10.5 Hz, 6H, −O*CH*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.6 (d, J_{C-F}=245.9 Hz), 137.3, 136.2, 131.8 (t, J_{C-F}=7.0 Hz), 130.6 (d, J_{C-P}=6.7 Hz), 127.0 (d, J_{C-P}=6.8 Hz), 121.2, 118.7, 114.4 (d, J_{C-F}=6.7 Hz), 114.0 (d, J_{C-P}=6.5 Hz), 109.0, 53.5 (d, J_{C-P}=7.9 Hz, −O*CH*$_3$), 51.6 (d, J_{C-P}=139.5 Hz, −*C*PO(OCH$_3$)$_2$), 32.8 (−NC*H*$_3$). Anal. Calcd for $C_{27}H_{26}FN_2O_3P$ (476.17): C, 68.06; H, 5.50; N, 5.88. Found: C, 68.22; H, 5.66; N, 5.59.

*3.2.4. Dimethyl (3-chlorophenyl)bis(1-methyl-1H-indol-3-yl) methylphosphonate (**3f**).* White needles, 271 mg (74%), mp 212–213 °C; R_f: 0.45 (EtOAc); IR (KBr): ν=3413, 3052, 2941, 1596, 1535, 1474, 1375, 1247, 1053, 1025, 820, 754 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$); δ 7.64 (dd, J=3.7 and 1.7 Hz, 1H), 7.48 (ddd, J=7.6, 4.3, and 1.7 Hz, 1H), 7.17–7.07 (m, 6H), 7.03 (t, J=8.1 Hz, 2H), 6.85 (d, J=2.4 Hz, 2H), 6.78 (t, J=8.1 Hz, 2H), 3.67 (s, 6H, −NC*H*$_3$), 3.41 (d, J=10.5 Hz, 6H, −O*CH*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.3 (d, J_{C-P}=4.4 Hz), 137.3, 133.6 (d, J_{C-P}=1.7 Hz), 130.7 (d, J_{C-P}=6.7 Hz), 130.1 (d, J_{C-P}=5.9 Hz), 128.8, 128.4 (d, J_{C-P}=6.3 Hz), 127.1, 127.0, 123.0, 121.3, 118.8, 113.5 (d, J_{C-P}=6.6 Hz), 109.0, 53.6 (d, J_{C-P}=7.9 Hz, −O*CH*$_3$), 52.2 (d, J_{C-P}=139.5 Hz, −*C*PO(OCH$_3$)$_2$), 32.9 (−NC*H*$_3$). Anal. Calcd for $C_{27}H_{26}ClN_2O_3P$ (492.14): C, 65.79; H, 5.320; N, 5.68. Found: C, 65.65; H, 5.46; N, 5.72.

*3.2.5. Dimethyl (4-chlorophenyl)bis(1-methyl-1H-indol-3-yl) methylphosphonate (**3g**).* Orange solid, 398.6 mg (81%), mp 233–234 °C; R_f: 0.25 EtOAc–hexane (4:1); IR (KBr): ν=3460, 2959, 1613, 1590, 1490, 1375, 1264, 1060, 1036, 810, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (dd, J=8.7 and 1.8 Hz, 2H), 7.20–7.09 (m, 6H), 7.05 (t, 2H, J=7.5 Hz), 6.90 (d, 2H, J=2.4 Hz), 6.79 (t, 2H, J=7.5 Hz), 3.65 (s, 6H, −NC*H*$_3$), 3.40 (d, J=10.5 Hz, 6H, −O*CH*$_3$), ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.2 (d, J_{C-P}=4.4 Hz), 137.4, 132.6, 131.6 (d, J_{C-P}=6.3 Hz), 130.7 (d, J_{C-P}=6.8 Hz), 127.8, 127.4 (d, J_{C-P}=6.8 Hz), 123.0, 122.3, 118.8, 113.0 (d, J_{C-P}=6.8 Hz), 107.0, 53.6 (d, J_{C-P}=7.8 Hz, −O*CH*$_3$), 51.9 (d, J_{C-P}=139.9 Hz, −*C*PO(OCH$_3$)$_2$), 32.9 (−NC*H*$_3$). Anal. Calcd for $C_{27}H_{26}ClN_2O_3P$ (492.14): C, 65.79; H, 5.32; N, 5.68. Found: C, 65.84; H, 5.44; N, 5.45.

*3.2.6. Dimethyl (4-methylphenyl)bis(1-methyl-1H-indol-3-yl)methylphosphonate (**3h**).* Yellow solid, 368 mg (78%), mp 228–229 °C; R_f: 0.25 EtOAc–hexane (4:1); IR (KBr): ν=3496, 2959, 1617, 1480, 1380, 1247, 1058, 1025, 804, 754 cm^{-1}; ^{1}H NMR: δ 7.46 (dd, J=8.3 and 1.7 Hz, 2H), 7.16–7.09 (m, 4H), 7.01–6.95 (m, 4H), 6.86 (d, J=2.4 Hz, 2H), 6.73 (t, J=7.4 Hz, 2H), 3.65 (s, 6H, −NC*H*$_3$), 3.38 (d, J=10.5 Hz, 6H, −O*CH*$_3$), 2.25 (s, −CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.3 (d, J_{C-P}=3.5 Hz), 136.2, 134.9 (d, J_{C-P}=3.5 Hz), 129.4 (d, J_{C-P}=6.8 Hz), 129.0 (d, J_{C-P}=6.2 Hz), 127.3, 126.2 (d, J_{C-P}=6.7 Hz), 122.2, 120.1, 117.6, 113.4 (d, J_{C-P}=6.5 Hz), 107.7, 52.3 (d, J_{C-P}=7.7 Hz, −O*CH*$_3$), 50.9 (d, J_{C-P}=138.3 Hz, −*C*PO(OCH$_3$)$_2$), 31.7 (−NC*H*$_3$), 28.6 (-*CH*$_3$). Anal. Calcd for $C_{28}H_{29}N_2O_3P$ (472.19): C, 71.17; H, 6.19; N, 5.93. Found: C, 71.24; H, 5.94; N, 5.67.

*3.2.7. Dimethyl (2-fluorophenyl)bis(1-methyl-1H-indol-3-yl) methylphosphonate (**3i**).* Violet needles, 323.7 mg (68%), mp 237–238 °C; R_f: 0.37 (EtOAc); IR (KBr): ν=3355, 2916, 1617, 1463, 1340, 1259, 1053, 1035, 810, 757 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 ((br t), J=7.4 Hz, 1H), 7.43 (d, J=8.3 Hz, 2H), 7.25–7.27 (m, 3H), 7.16 (t, J=7.4 Hz, 2H), 7.07 (t, J=7.6 Hz, 1H), 6.98–6.91 (m, 5H), 3.69 (s, 6H, −NC*H*$_3$), 3.44 (d, J=10.6 Hz, 6H, −O*CH*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.5 (dd, J_{C-F}=251.5 Hz and J_{C-P}=8.0 Hz), 137.3, 131.9 (dd, J_{C-F}=5.9 Hz and J_{C-P}=3.2 Hz), 130.3 (d, J_{C-F}=7.4 Hz), 129.1 (d, J_{C-P}=8.5 Hz), 128.8 (d, J_{C-F}=10.8 Hz and J_{C-P}=3.4 Hz), 127.0 (d, J_{C-F}=10.8 Hz), 123.4 (d, J_{C-F}=2.9 Hz), 122.9, 121.1, 118.7, 116.4 (d, J_{C-F}=23.7Hz), 113.5 (d, J_{C-P}=7.0 Hz), 108.9, 53.5 (d, J_{C-P}=7.9 Hz, −O*CH*$_3$), 50.7 (J_{C-P}=142.5 Hz, −*C*PO(OCH$_3$)$_2$), 32.8 (−NC*H*$_3$). Anal. Calcd for $C_{27}H_{26}FN_2O_3P$ (476.17): C, 68.06; H, 5.50; N, 5.88. Found: C, 68.23; H, 5.29; N, 5.59.

*3.2.8. Dimethyl 1,1- bis(1-methyl-1H-indol-3-yl) ethylphosphonate (**3j**).* Orange solid, 305 mg (77%), mp140–141 °C; R_f: 0.20 (EtOAc); IR (KBr): ν=2925, 1470, 1380, 1264, 1107, 1031, 811 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15 (d, J=2.2 Hz, 2H) 7.11 ((br t), J=7.3 Hz, 4H), 7.00 (t, J=7.9 Hz, 2H), 6.70 (t, J=7.7 Hz, 2H), 3.63 (s, 6H, −NC*H*$_3$), 3.46 (d, J=10.5 Hz, 6H, −O*CH*$_3$), 2.11 (d, J=16.5 Hz, 3H, −*CH*$_3$), ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.1, 128.0 (d, J_{C-P}=6.3 Hz), 126.8 (d, J_{C-P}=8.7 Hz), 121.5, 120.9, 118.4, 114.5 (d, J_{C-P}=5.3 Hz), 108.8, 53.2 (d, J_{C-P}=7.7 Hz, −O*CH*$_3$), 40.8 (d, J_{C-P}=141.9 Hz, −*C*PO(OCH$_3$)$_2$), 32.6 (−NC*H*$_3$) 25.4 (d, J_{C-P}=198.9 Hz, −*CH*$_3$). Anal. Calcd for $C_{22}H_{25}N_2O_3P$ (396.16): C, 66.66; H, 6.36; N, 7.07. Found: C, 66.23; H, 6.27; N, 7.28.

*3.2.9. Dimethyl 1,1-bis(1-methyl-1H-indol-3-yl) propylphosphonate (**3k**).* Yellow needles, 291 mg (71%), mp 96–97 °C; R_f: 0.25 EtOAc–hexane (4:1); IR (KBr): ν=2941, 1474, 1336, 1236, 1058, 1042, 820 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 (d, J=2.3 Hz, 2H), 7.11 (d, J=8.1 Hz, 2H), 6.96–6.90 (m, 4H), 6.62 (t, J=7.5 Hz, 2H), 3.72 (s, +−NC*H*$_3$, 6H), 3.42 (d, J=10.4 Hz, 6H, −O*CH*$_3$), 2.64 (qd, J=7.3 and J=18.6 Hz, 1H), 0.79 (t, J=7.3 Hz, 3H, −CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.0, 129.2 (d, J_{C-P}=6.1 Hz), 127.6 (d, J_{C-P}=8.9 Hz), 122.0, 121.1, 118.6, 112.7 (d, J_{C-P}=6.4 Hz), 53.1 (d, J_{C-P}=7.8 Hz, −O*CH*$_3$), 46.1 (d, J_{C-P}=138.7 Hz, −*C*PO(OCH$_3$)$_2$), 32.9 (−NC*H*$_3$), 29.7 (d, J_{C-P}=2.0 Hz, -*CH*$_2$CH$_3$), 10.1 (d, J_{C-P}=5.1 Hz, −CH$_2$*CH*$_3$). Anal. Calcd for $C_{23}H_{27}N_2O_3P$ (410.18): C, 67.30; H, 6.63; N, 6.83. Found: C, 69.11; H, 6.48; N, 6.92.

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Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2011.03.061. These data include MOL files and InChIKeys of the most important compounds described in this article.

References and notes

1. (a) Kam, T. S. In *Alkaloids, Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Pergamon: Amsterdam, 1999; Vol. 4, p 429; (b) Bradfield, C. A.; Bjeldanes, L. F. *J. Toxicol. Environ. Health* **1987**, *21*, 311–313; (c) Dashwood, R. H.; Uyetake, L.; Fong, A. T.; Hendricks, J. D.; Bailey, G. S. *Food Chem. Toxicol.* **1987**, *27*, 385–392.
2. (a) Morris, S. A.; Anderson, R. A. *Tetrahedron* **1990**, *46*, 715–720; (b) Umezawa, K.; Tangiguchi, T.; Toi, M.; Ohse, T.; Ishutsumi, T.; Yamamoto, T.; Koyano, T.; Ishizuka, M. *Drugs Exp. Clin. Res.* **1996**, *22*, 35–40; (c) Amino, N.; Ohse, T.; Koyano, T.; Umezawa, K. *Anticancer Res.* **1996**, *16*, 55–59; (d) Bifulco, G.; Bruno, I.; Riccio, R.; Lavayre, J.; Bourdy, G. *J. Nat. Prod.* **1995**, *58*, 1254–1260; (e) Umezawa, K.; Ohse, T.; Koyano, T.; Takahashi, Y. *Anticancer Res.* **1994**, *14*, 2413–2417.
3. (a) Ji, S.-J.; Zhon, M.-F.; Gu, D.-G.; Wang, S. Y.; Loh, T.-P. *Synlett* **2003**, 2077–2079; (b) Nagarajan, R.; Perumal, P. T. *Tetrahedron* **2002**, *58*, 1229–1232; (c) Yadav, JS.; Subba Reddy, B. V.; Murthy, C. V. S. R.; Madan, C. *Synthesis* **2001**, 783–787; (d) Chen, D.; Yu, L.; Wang, P. G. *Tetrahedron Lett.* **1996**, *37*, 4467–4470; (e) Earle, M. J.; Fairhurst, R. A.; Heaney, H. *Tetrahedron Lett.* **1991**, *32*, 6171–6174; (f) Ji, S.-J.; Zhou, M.-F.; Gu, D.-G.; Jiang, Z.-Q.; Loh, T.-P. *Eur. J. Org. Chem.* **2004**, 1584–1587; (g) Bartoli, G.; Bosco, M.; Foglia, G.; Giuliani, A.; Marcantoni, E.; Sambri, L. *Synthesis* **2004**, 895–900.
4. (a) Mahadevan, A.; Sard, H.; Gonzalez, M.; McKew, J. C. *Tetrahedron Lett.* **2003**, *44*, 4589–4591; (b) Chakrabarty, M.; Ghosh, N.; Basak, R.; Harigaya, Y. *Tetrahedron Lett.* **2002**, *43*, 4075–4078.
5. (a) Mi, X.; Luo, S.; He, J.; Cheng, J.-P. *Tetrahedron Lett.* **2004**, *45*, 4567–4570; (b) Bandgar, B. P.; Shaikh, K. A. *Tetrahedron Lett.* **2003**, *44*, 1959–1961; (c) Yadav, J. S.; Reddy, B. V. S.; Padmavani, B.; Gupta, M. K. *Tetrahedron Lett.* **2004**, *45*, 7577–7579; (d) Ünaleroglu, C.; Temelli, B.; Demir, A. S. *Synthesis* **2004**, *15*, 2574–2578.
6. (a) Demir, A. S.; Esiringu, I.; Gollu, M.; Reis, O. *J. Org. Chem.* **2009**, *74*, 2197–2199; (b) Demir, A. S.; Reis, Ö; İgdir, Ç; Esiringü, I.; Eymur, S. *J. Org. Chem.* **2005**, *70*, 10584–10587; (c) Demir, A. S.; Eymur, S. *J. Org. Chem.* **2007**, *77*, 8527–8530; (d) Demir, A. S.; Reis, B.; Reis, Ö; Eymür, S.; Göllü, M.; Tural, S.; Saglam, G. *J. Org. Chem.* **2007**, *72*, 7439–7442; (e) Demir, A. S.; Akhmedov, I. M.; Sesenoglu, O. *Tetrahedron* **2002**, *58*, 9793–9799; (f) Demir, A. S.; Sesenoglu, O.; Gercek-Arkin, Z. *Tetrahedron: Asymmetry* **2001**, *12*, 2309–2313.
7. (a) Demir, A. S.; Aybey, A.; Emrullahoglu, M. *Synthesis* **2009**, *10*, 1655–1658; (b) Demir, A. S.; Emrullahoglu, M.; Pirkin, E.; Akca, N. *J. Org. Chem.* **2008**, *73*, 8992–8997; (c) Demir, A. S.; Reis, Ö; Kayalar, M.; Eymur, S.; Reis, B. *Synlett* **2006**, *19*, 3329–3333; (d) Demir, A. S.; Reis, Ö; Esiringü, I.; Reis, B.; Baris, S. *Tetrahedron* **2007**, *63*, 160–165.
8. Mitsuo, S.; Masaki, S.; Hikaru, Y.; Tsujiaki, H. *J. Org. Chem.* **1980**, *45*, 4162–4167.