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Synthesis of Aziridine- and Oxirane-2-phosphonates Spiro-Fused with Oxindoles

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Dedicated to Professor P. Antonio Tardella on the occasion of his 75th birthday

Keywords: Epoxidation / Heterocycles / Indoles / Small ring systems / Spiro compounds / Wittig reactions

3-(Phosphorylmethylene)oxindoles have been prepared by a straightforward Horner–Wadsworth–Emmons reaction. They were treated with ethyl *N*-{[(4-nitrophenyl)sulfonyl]oxy}-carbamate ($NsONHCO_2Et$) in the presence of CaO to afford new aziridine-2-phosphonates spiro-fused with oxindole. 3-(Phosphorylmethylene)oxindoles were also transformed into novel spiro[oxindole-oxiranes] by reaction with H_2O_2/NaOH.

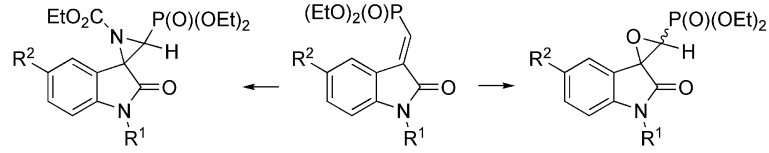
Introduction

The synthesis of molecules containing a spiroheterocycle moiety has been widely reported.[1] Due to steric strain, the presence of a spiro carbon atom induces easy rearrangements that can lead to different heterocyclic derivatives. Numerous spirocyclic alkaloids and pharmacologically important compounds have a central skeleton based on the spirooxindole system.[2] Spiro[oxindole-oxirane] ring systems are also of particular interest because of their biological applications as anticonvulsants, diuretics, sedatives, antifungal, and antitubercular agents.[3]

In contrast, spiro[aziridine-oxindoles] have not been much studied. We have recently reported a novel synthesis of these compounds from oxindoles bearing a methylene or a vinylcarboxylate group in the α-position.[4] The employed methodology has already been successfully used in our research group for the preparation of *N*-(ethoxycarbonyl)-aziridines from electron-poor olefins, such as α,β-unsaturated esters and phosphonates.[5]

1 2

Figure 1. Clinically important aziridine- and oxirane-2-phosphonates.



3 5 4

Figure 2. Synthesis of compounds **3** and **4** by starting from oxindoles **5**.

Herein, we focused our attention on the synthesis of new aziridine-2-phosphonates spirofused with oxindoles and investigated the possibility of obtaining analogous spiro-[oxindole-oxirane]–phosphonates.

Aziridine- and oxirane-2-phosphonates are important classes of compounds, and much interest has focused on the biological activity of some derivatives.[6] For instance, (1,2-epoxypropyl)phosphonic acid (**1**; Fosfomycin)[7] is a clinically important drug with wide-spectrum antibiotic activity

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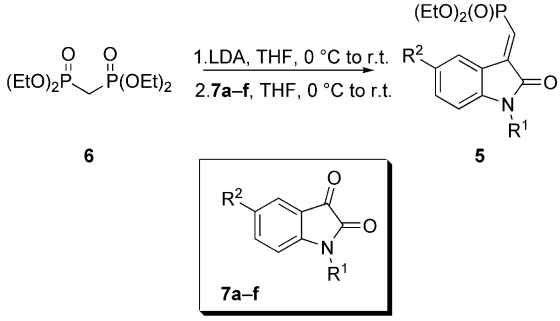
(Figure 1), whereas 1-alkoxycarbonyl-2-phosphonoaziridines (**2**) show antibacterial activity.[8] Aziridine- and oxiranephosphonates can be also regarded as useful precursors of a multitude of amino acid mimics after ring opening.[9]

In order to achieve our goal, we designed the synthesis of compounds **3** and **4** starting from oxindoles **5** bearing a phosphorylmethylene group in the 3-position (Figure 2).

Results and Discussion

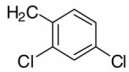
Keeping in mind this program, our first objective was the preparation of substrates **5a**–**f** (Scheme 1), which were obtained through the Horner–Wadsworth–Emmons reaction,[10] starting from tetraethyl methylenebis(phosphonate) (**6**) and isatine derivatives **7a**–**f** having different substituents either on the nitrogen atom (R^1) or on the aromatic ring (R^2).



Scheme 1. Synthesis of 3-(phosphorylmethylene)oxindoles **5a**–**f**.

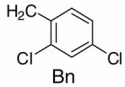
Reasonably good results were achieved with tetrahydrofuran (THF) as solvent and lithium diisopropylamide (LDA) as base (Table 1). The main products, which were purified by chromatography on silica gel (hexane/ethyl acetate), were always the thermodynamically more stable (*E*) isomers; their structures were confirmed by ^{1}H NMR spectroscopic analysis. Indeed, as reported for the (*E*) isomers of the analogous 3-(oxycarbonylmethylene)oxindoles,[11] the electronic effect of the phosphonate group markedly deshields the 4-H atom with respect to the other aromatic protons.

Table 1. Synthesis of 3-(phosphorylmethylene)oxindoles **5a**–**f**.

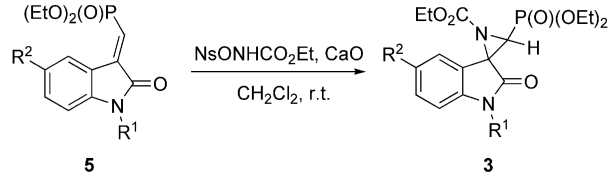
Entry	7	R^1	R^2	Yield **5** (*E*) [%]
1	**a**	CH_3	H	66
2	**b**	Ph	H	76
3	**c**		H	72
4	**d**	Bn	H	56
5	**e**	Bn	OCH_3	70
6	**f**	Bn	$CH(CH_3)_2$	67

With these new unsaturated phosphonates in hand, we performed the aziridination reactions with substrates **5a**–**f** in CH_2Cl_2 using the procedure developed previously. Unlike the aziridination of previously studied α,β-unsaturated phosphonates,[5] only 1 or 2 equiv. (Table 2, Entries 1–3 or 4–6) of $NsONHCO_2Et$ and CaO was necessary for complete disappearance of the starting material and formation of the expected *N*-(ethoxycarbonyl)aziridine spiro compounds **3a**–**f** (Scheme 2).

Table 2. Synthesis of spiro[aziridine-oxindoles] **3a**–**f**.

Entry	5	R^1	R^2	Molar ratio[a]	Yield **3** [%]
1	**a**	CH_3	H	1:1:1	30
2	**b**	Ph	H	1:1:1	42
3	**c**		H	1:1:1	29
4	**d**	Bn	H	1:2:2	33
5	**e**	Bn	OCH_3	1:2:2	32
6	**f**	Bn	$CH(CH_3)_2$	1:2:2	48

[a] Ratio of **5**/$NsONHCO_2Et$/CaO.



Scheme 2. Synthesis of spiro[aziridine-oxindoles] **3a**–**f**.

In all cases, the crude ^{1}H NMR spectra indicated the formation of a single isomer, as evidenced by the presence of a unique aziridine proton signal, which appeared as a broad doublet ($J \approx 17$ Hz, $\delta = 3$–3.5 ppm) due to the characteristic coupling with the phosphorus atom. After chromatography, products **3a**–**f** were isolated in the reported yields (Table 2) and fully characterized. The stereochemistry of the starting ylidenephosphonate was fully retained in the products, which was clearly shown by ^{1}H NMR spectroscopic analysis. Indeed, in the region of the aromatic protons, the characteristic signal from the highly deshielded 4-H atom was still present. Moreover, the same stereochemical outcome was previously observed in the aziridination of α,β-unsaturated phosphonates.[5] Yields of the isolated compounds were modest; however, their ^{1}H NMR spectroscopic analysis matched those of the corresponding spectra of the crude products (70–80% yield).

Concerning the synthesis of spiro-oxirane–phosphonates, we chose to use classic epoxidation reagents (H_2O_2, NaOH), which are usually employed for the preparation of simple epoxyoxindoles,[12] even though a very poor reactivity of ylidenephosphonates under such reaction conditions has been reported.[13] The principal synthetic routes to (1,2-epoxyalkyl)phosphonates include: the treatment of halohydrines with a base, the reaction of α-halo ketones or α-tosyloxy ketones with alkali metal derivatives of dialkyl phosphonates, or the application of Darzens-type reactions of (halomethyl)phosphonates with aldehydes or ketones.[14]

Using the basic oxidizing conditions (3 equiv. of 30% hydrogen peroxide and 0.2 equiv. of sodium hydroxide), we observed an immediate decolourization of the red starting solution and, in all cases, the reactions were complete within 2 h (Scheme 3).

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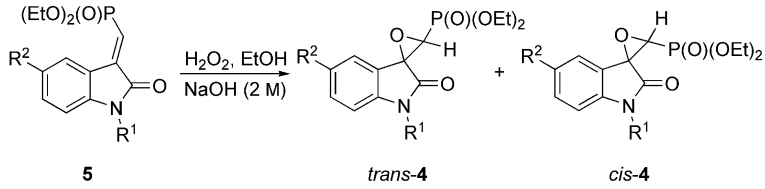


Scheme 3. Synthesis of spiro[oxindole-oxiranes] **4a**–**f**.

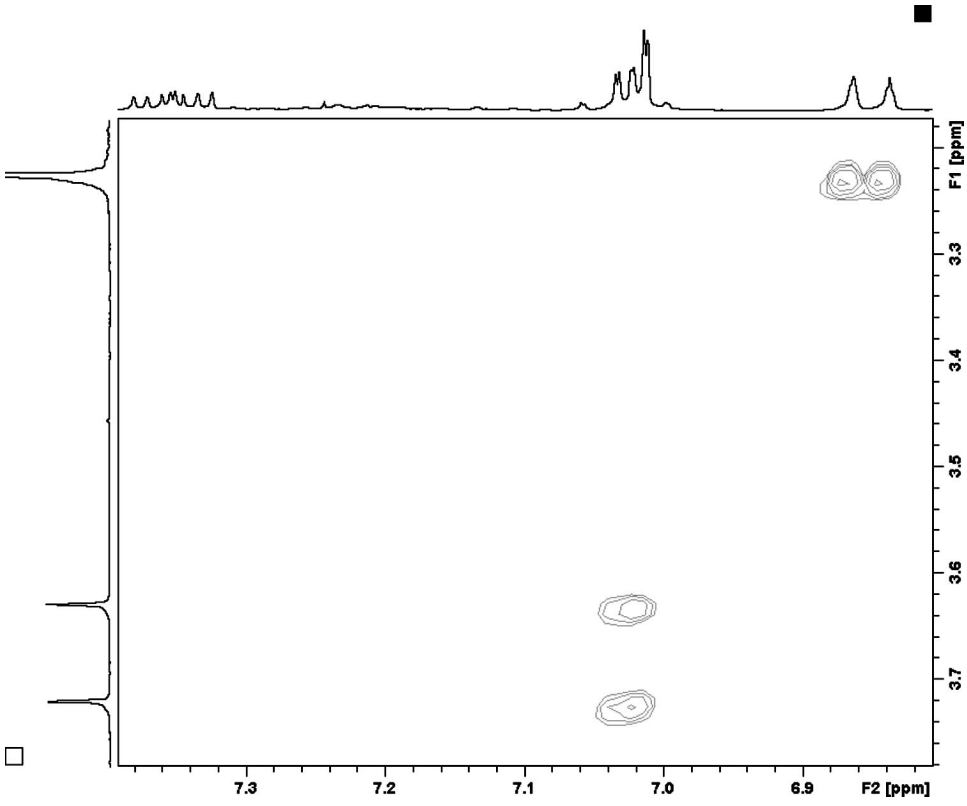
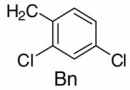


Figure 3. NOESY spectrum of *cis*-**4a**.

^{1}H NMR analysis revealed the formation of the *trans* and *cis* diastereomeric spiro-oxiran-2-phosphonates **4**. The two products were separated by chromatography (hexane/ethyl acetate), and the minor product was identified as the *cis* isomer by NOESY spectroscopic analysis of **4a**. Indeed, NOESY cross peaks were found between the aromatic 4-H atom (δ = 7.04 ppm) and the epoxide proton (Figure 3). In contrast, no NOESY cross peaks for the epoxide proton were found in the major *trans* isomer **4a**. In addition, typical ^{1}H NMR spectral patterns of the aromatic protons were observed for all the *trans* isomers. The yields and the ratios of the two epoxides are reported in Table 3.

Table 3. Synthesis of spiro[oxindole-oxiranes] **4a**–**f**.

Entry	5	R^1	R^2	Yield 4 [%]	*trans*/*cis*
1	**a**	CH_3	H	80	78:22
2	**b**	Ph	H	78	80:20
3	**c**		H	89	75:25
4	**d**	Bn	H	80	85:15
5	**e**	Bn	OCH_3	96	83:17
6	**f**	Bn	$CH(CH_3)_2$	92	92:8

Conclusion

We propose two straightforward approaches to new spiro-oxindole derivatives; in particular, aziridine- and oxirane-2-phosphonates were obtained with moderate to high yields. The syntheses are stereoselective, and further enantioselective reactions are under investigation. The obtained compounds are potentially biologically active and constitute key intermediates for the synthesis of hydroxy or amino phosphonate derivatives.

Experimental Section

General Experimental Methods: Solvents and common reagents were purchased from commercial sources and used without further purification. All reactions were monitored by thin layer chromatography (TLC) carried out on Merck F-254 silica glass plates and

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visualized with UV light. ^{1}H NMR spectra were recorded with a Varian Gemini 200 (200 MHz) spectrometer. Chemical shifts (δ) are expressed in parts per million (ppm) and are referenced to the residual protons of the NMR solvent ($CHCl_3$: δ = 7.26 ppm); s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sept = septuplet, dd = double doublet, dt = double triplet, m = multiplet. Coupling constants (J) are expressed in Hz. ^{13}C NMR spectra were recorded with a Varian Gemini 300 (75 MHz) spectrometer. Chemical shifts (δ) are expressed in parts per million (ppm) and are referenced to the residual carbon atoms of the NMR solvent ($CHCl_3$: δ = 77.0 ppm). ^{31}P NMR spectra were obtained in $CDCl_3$ with a Bruker AC 400 spectrometer, with H_3PO_4 as external standard. NOESY experiments were recorded with a Bruker AC 300 spectrometer. Infrared (IR) spectra were obtained by using a Perkin–Elmer 1600 (FTIR) spectrometer; data are presented as wavenumbers (cm^{-1}). HRMS spectra were recorded with a Micromass Q-TOF Micromass Spectrometer (Waters), coupled to a Micromass LCT (ESI) with lock spray injector (injection loop mode in an HPLC system, Waters, Alliance 2695).

General Procedure for the Horner–Wadsworth–Emmons Reaction: To a stirred solution of tetraethyl methylenebis(phosphonate) (**1**; 2.6 mmol, 749 mg) in anhydrous THF (2 mL) under Ar at 0 °C, LDA (2 M in THF, 1.43 mL, 2.86 mmol) was added dropwise. After 30 min, the mixture was warmed to room temp., stirred for an additional 30 min and cooled again to 0 °C. At this temperature, a solution of isatine **7** (2 mmol) in anhydrous THF (8 mL) was slowly added. The reaction mixture was allowed to reach room temp., and stirred until complete (monitored by TLC; hexane/ethyl acetate). Saturated aqueous NH_4Cl salution was slowly added, and the aqueous layer was extracted with ethyl acetate (3 × 50 mL). The combined organic phases were dried with anhydrous Na_2SO_4 and concentrated under reduced pressure to give the crude product, which was subsequently purified by flash chromatography on silica gel (hexane/ethyl acetate).

Diethyl {[(3*E*)-1-Methyl-2-oxoindolin-3-ylidene]methyl}phosphonate (5a): Yield: 390 mg (1.32 mmol, 66%); pale-orange solid; isolated as a single (*E*) isomer; R_f = 0.36 (hexane/ethyl acetate, 1:1). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.33 (t, J = 7.1 Hz, 3 H, CH_3CH$_2$O), 1.34 (t, J = 7.1 Hz, 3 H, CH_3CH$_2$O), 3.22 (s, 3 H, CH_3N), 4.06–4.23 [m, 4 H, (CH$_3$CH_2O)$_2$P], 6.78 (d, J = 7.6 Hz, 1 H, ArH), 6.80 (d, $J_{H,P}$ = 13.4 Hz, 1 H, CHP=O), 7.06 (dt, J = 7.6, 1.1 Hz, 1 H, ArH), 7.36 (m, 1 H, ArH), 8.45 (d, J = 7.6 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 16.2 (d, J_{CCOP} = 6.4 Hz), 26.3, 62.5 (d, J_{COP} = 5.7 Hz), 108.1, 119.6 (d, J_{CP} = 189.6 Hz), 119.9 (d, J_{CCP} = 7.0 Hz), 123.0, 127.9, 132.2, 141.6 (d, J_{CCCP} = 7.7 Hz), 145.8, 166.6 (d, J_{CCCP} = 25.7 Hz) ppm. ^{31}P NMR: δ = 14.2 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1713, 1236 cm^{-1}. HRMS: calcd. for $C_{14}H_{18}NNaO_4P$ 318.0871; found 318.0868.

Diethyl {[(3*E*)-2-Oxo-1-phenylindolin-3-ylidene]methyl}phosphonate (5b): Yield: 543 mg (1.52 mmol, 76%); pale-orange solid; isolated as a single (*E*) isomer; R_f = 0.45 (hexane/ethyl acetate, 1:1). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.21 [t, J = 7.1 Hz, 6 H, (CH_3CH$_2$O)$_2$P], 4.13–4.28 [m, 4 H, (CH$_3$CH_2O)$_2$P], 6.78 (d, J = 7.9 Hz, 1 H, ArH), 6.91 (d, $J_{H,P}$ = 13.1 Hz, 1 H, CHP=O), 7.10 (dt, J = 7.7, 1.0 Hz, 1 H, ArH), 7.24–7.33 (m, 1 H, ArH), 7.37–7.46 (m, 3 H, ArH), 7.49–7.58 (m, 2 H, ArH), 8.55 (d, J = 7.7 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 16.3 (d, J_{CCOP} = 6.3 Hz), 62.5 (d, J_{COP} = 5.7 Hz), 109.5, 119.9 (d, J_{CCP} = 6.8 Hz), 120.1 (d, J_{CP} = 189.7 Hz), 122.0, 123.4, 128.1, 128.3, 129.7, 132.1, 134.0, 141.3 (d, J_{CCCP} = 7.8 Hz), 145.8, 165.9 (d, J_{CCCP} = 25.9 Hz) ppm. ^{31}P NMR: δ = 14.1 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1720, 1236 cm^{-1}. HRMS: calcd. for $C_{19}H_{20}NNaO_4P$ 380.1028; found 380.1023.

Diethyl {[(3*E*)-1-(2,4-Dichlorobenzyl)-2-oxoindolin-3-ylidene]methyl}phosphonate (5c): Yield: 634 mg (1.44 mmol, 72%); orange solid; isolated as a single (*E*) isomer; R_f = 0.42 (hexane/ethyl acetate, 1:1). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.37 [t, J = 7.1 Hz, 6 H, (CH_3CH$_2$O)$_2$P], 4.10–4.27 [m, 4 H, (CH$_3$CH_2O)$_2$P], 5.00 (s, 2 H, CH_2N), 6.62 (d, J = 7.8 Hz, 1 H, ArH), 6.89 (d, $J_{H,P}$ = 13.0 Hz, 1 H, CHP=O), 7.01–7.18 (m, 4 H, ArH), 7.23–7.32 (m, 1 H, ArH), 8.51 (d, J = 7.6 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 16.3 (d, J_{CCOP} = 6.4 Hz), 40.9 (NCH_2), 62.5 (d, J_{COP} = 5.7 Hz), 109.0, 119.9 (d, J_{CP} = 189.6 Hz), 120.3 (d, J_{CCP} = 6.9 Hz), 123.4, 127.5, 128.0, 128.8, 129.5, 131.3, 132.3, 133.4, 134.1, 140.9 (d, J_{CCCP} = 7.7 Hz), 144.3, 166.8 (d, J_{CCCP} = 25.8 Hz) ppm. ^{31}P NMR: δ = 13.8 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1717, 1237 cm^{-1}. HRMS: calcd. for $C_{20}H_{20}Cl_2NNaO_4P$ 462.0405; found 462.0402.

Diethyl {[(3*E*)-1-Benzyl-2-oxoindolin-3-ylidene]methyl}phosphonate (5d): Yield: 416 mg (1.12 mmol, 56%); orange solid; isolated as a single (*E*) isomer; R_f = 0.46 (hexane/ethyl acetate, 1:1). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.36 [t, J = 7.0 Hz, 6 H, (CH_3CH$_2$O)$_2$P], 4.07–4.26 [m, 4 H, (CH$_3$CH_2O)$_2$P], 4.93 (s, 2 H, CH_2N), 6.69 (d, J = 7.9 Hz, 1 H, ArH), 6.88 (d, $J_{H,P}$ = 13.3 Hz, 1 H, CHP=O), 7.04 (dt, J = 7.7, 0.96 Hz, 1 H, ArH), 7.21–7.34 (m, 6 H, ArH), 8.47 (d, J = 7.7 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 16.1 (d, J_{CCOP} = 6.3 Hz), 62.3 (d, J_{COP} = 5.7 Hz), 109.0, 119.7 (d, J_{CCP} = 6.8 Hz), 120.5 (d, J_{CP} = 189.8 Hz), 122.8, 127.1, 127.5, 127.6, 128.6, 132.0, 135.2, 141.2 (d, J_{CCCP} = 7.7 Hz), 144.7, 166.4 (d, J_{CCCP} = 25.7 Hz) ppm. ^{31}P NMR: δ = 14.1 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1714, 1236 cm^{-1}. HRMS: calcd. for $C_{20}H_{22}NNaO_4P$ 394.1184; found 394.1181.

Diethyl {[(3*E*)-1-Benzyl-5-methoxy-2-oxoindolin-3-ylidene]methyl}-phosphonate (5e): Yield: 562 mg (1.40 mmol, 70%); orange solid; isolated as a single (*E*) isomer; R_f = 0.42 (hexane/ethyl acetate, 3:7). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.37 [t, J = 7.1 Hz, 6 H, (CH_3CH$_2$O)$_2$P], 3.79 (s, 3 H, CH_3O), 4.12–4.27 [m, 4 H, (CH$_3$CH_2O)$_2$P], 4.90 (s, 2 H, CH_2N), 6.57 (d, J = 8.6 Hz, 1 H, ArH), 6.73–6.83 (m, 1 H, ArH), 6.87 (d, J_{HP} = 13.0 Hz, 1 H, CHP=O), 7.27–7.33 (m, 5 H, ArH), 8.24 (d, J = 2.6 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 16.4 (d, J_{CCOP} = 6.5 Hz), 44.1, 55.9, 62.5 (d, J_{COP} = 5.8 Hz), 109.8, 113.3, 118.7, 119.9 (d, J_{CP} = 189.3 Hz), 120.7 (d, J_{CCP} = 6.7 Hz), 121.2, 127.3, 127.8, 128.8, 135.5, 138.4, 156.1, 166.5 (d, J_{CCCP} = 25.4 Hz) ppm. ^{31}P NMR: δ = 14.3 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1715, 1236 cm^{-1}. HRMS: calcd. for $C_{21}H_{24}NNaO_5P$ 424.1290; found 424.1286.

Diethyl {[(3*E*)-1-Benzyl-5-isopropyl-2-oxoindolin-3-ylidene]methyl}-phosphonate (5f): Yield: 554 mg (1.34 mmol, 67%); orange solid; isolated as a single (*E*) isomer; R_f = 0.46 (hexane/ethyl acetate, 1:1). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.22 [d, J = 6.9 Hz, 6 H, (CH_3)$_2$CH], 1.36 [t, J = 7.1 Hz, 6 H, (CH_3CH$_2$O)$_2$P], 2.88 [quint, J = 6.9 Hz, 1 H, (CH$_3$)$_2$CH], 4.12–4.27 [m, 4 H, (CH$_3$CH_2O)$_2$P], 4.91 (s, 2 H, CH_2N), 6.60 (d, J = 8.1 Hz, 1 H, ArH), 6.86 (d, $J_{H,P}$ = 13.7 Hz, 1 H, CHP=O), 7.08–7.13 (m, 1 H, ArH), 7.29–7.34 (m, 5 H, ArH), 8.36 (d, J = 1.7 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 16.3 (d, J_{CCOP} = 6.4 Hz), 24.0, 33.7, 43.9, 62.3 (d, J_{COP} = 5.8 Hz), 108.9, 119.1 (d, J_{CP} = 189.4 Hz), 119.9 (d, J_{CCP} = 6.8 Hz), 125.9, 127.2, 127.6, 128.7, 130.1, 135.5, 141.8 (d, J_{CCCP} = 7.8 Hz), 142.9, 143.7, 166.7 (d, J_{CCCP} = 25.7 Hz) ppm. ^{31}P NMR: δ = 14.4 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1712, 1236 cm^{-1}. HRMS: calcd. for $C_{23}H_{28}NNaO_4P$ 436.1654; found 436.1651.

General Procedure for the Aziridination Reaction: To a stirred solution of 3-methyleneoxindole **5** (1 mmol) in CH_2Cl_2 (1 mL), NsONHCO$_2$Et (290 mg, 1 mmol), and CaO (56 mg, 1 mmol) were added portionwise at room temp. every hour, until the molar ratio of **5**/NsONHCO$_2$Et/CaO reported in Table 2 was reached. Because

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the reaction is exothermic, during each addition the flask was cooled in a water bath to avoid overheating. After 24 h, the reaction was quenched by adding pentane/CH_2Cl_2 (8:2). The resulting solid by-product was filtered and washed with the same solution. The organic phase was concentrated under reduced pressure and dried with anhydrous Na_2SO_4. The crude mixture was purified by chromatography on silica gel (hexane/ethyl acetate).

Ethyl 3-(Diethoxyphosphoryl)-1′-methyl-2′-oxospiro[aziridine-2,3′-indoline]-1-carboxylate (3a): Yield: 116 mg (0.30 mmol, 30%); yellow solid; isolated as the *trans* isomer; R_f = 0.40 (hexane/ethyl acetate, 2:8). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.16 [t, J = 7.1 Hz, 3 H, (CH_3CH$_2$O)$_2$P], 1.25 [t, J = 7.1 Hz, 3 H, (CH_3CH$_2$O)$_2$P], 1.42 (t, J = 7.1 Hz, 3 H, CH_3CH$_2$OC), 3.29 (s, 3 H, NCH_3), 3.32 (d, $J_{H,P}$ = 17.4 Hz, 1 H, NCH), 3.98–4.10 [m, 2 H, (CH$_3$CH_2O)$_2$P], 4.21 (q, J = 7.1 Hz, 2 H, CH$_3$CH_2O), 4.28–4.42 [m, 2 H, (CH$_3$CH_2O)$_2$P], 6.92 (d, J = 7.7 Hz, 1 H, ArH), 7.12 (dt, J = 7.7, 1.0 Hz, 1 H, ArH), 7.39 (dt, J = 7.7, 1.3 Hz, 1 H, ArH), 7.92 (d, J = 7.7 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 14.4, 16.4 (d, J_{CCOP} = 5.8 Hz), 16.6 (d, J_{CCOP} = 5.9 Hz), 27.1, 44.4 (d, J_{CP} = 207.8 Hz), 48.4 (d, J_{CCP} = 4.5 Hz), 62.9 (d, J_{COP} = 6.3 Hz), 63.6, 63.7 (d, J_{COP} = 4.8 Hz), 108.7, 121.1, 123.3, 126.4, 130.4, 145.2, 159.4, 169.6 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1740, 1722, 1257 cm^{-1}. HRMS: calcd. for $C_{17}H_{23}N_2NaO_6P$ 405.1191; found 405.1188.

Ethyl 3-(Diethoxyphosphoryl)-2′-oxo-1′-phenylspiro[aziridine-2,3′-indoline]-1-carboxylate (3b): Yield: 187 mg (0.42 mmol, 42%); yellow solid; isolated as the *trans* isomer; R_f = 0.44 (hexane/ethyl acetate, 2:8). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.14–1.31 [m, 6 H, (CH_3CH$_2$O)$_2$P], 1.45 (t, J = 7.0 Hz, 3 H, CH_3CH$_2$OC), 3.41 (d, $J_{H,P}$ = 17.3 Hz, 1 H, NCH), 3.97–4.47 [m, 6 H, (CH$_3$CH_2O)$_2$P, CH$_3$CH_2O], 6.88 (d, J = 7.7 Hz, 1 H, ArH), 7.15 (t, J = 7.7 Hz, 1 H, ArH), 7.27–7.36 (m, 1 H, ArH), 7.38–7.48 (m, 3 H, ArH), 7.49–7.62 (m, 2 H, ArH), 7.98 (d, J = 7.7 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 14.5, 16.4 (d, J_{CCOP} = 5.3 Hz), 16.6 (d, J_{CCOP} = 6.6 Hz), 44.9 (d, J_{CP} = 207.8 Hz), 48.6 (d, J_{CCP} = 4.2 Hz), 63.0 (d, J_{COP} = 6.1 Hz), 63.7, 63.8 (d, J_{COP} = 5.6 Hz), 110.0, 121.0, 123.8, 126.7, 126.8, 128.7, 129.9, 130.0, 130.3, 134.1, 145.4, 159.3, 169.2 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1732, 1720, 1256 cm^{-1}. HRMS: calcd. for $C_{22}H_{25}N_2NaO_6P$ 467.1348; found 467.1344.

Ethyl 1′-(2,4-Dichlorobenzyl)-3-(diethoxyphosphoryl)-2′-oxospiro[aziridine-2,3′-indoline]-1-carboxylate (3c): Yield: 153 mg (0.29 mmol, 29%); yellow solid; isolated as the *trans* isomer; R_f = 0.43 (hexane/ethyl acetate, 2:8). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.18 [t, J = 7.1 Hz, 3 H, (CH_3CH$_2$O)$_2$P], 1.24 [t, J = 7.1 Hz, 3 H, (CH_3CH$_2$O)$_2$P], 1.44 (t, J = 7.1 Hz, 3 H, CH_3CH$_2$OC), 3.41 (d, $J_{H,P}$ = 17.2 Hz, 1 H, NCH), 3.96–4.12 [m, 2 H, (CH$_3$CH_2O)$_2$P], 4.21 (q, J = 7.1 Hz, 2 H, CH$_3$CH_2O), 4.29–4.44 [m, 2 H, (CH$_3$CH_2O)$_2$P], 4.94 (d, J = 16.6 Hz, 1 H, NCH$_a$$H_b$), 5.16 (d, J = 16.6 Hz, 1 H, NCH_aH$_b$), 6.71 (d, J = 7.4 Hz, 1 H, ArH), 7.04 (t, J = 7.8 Hz, 1 H, ArH), 7.12–7.19 (m, 2 H, ArH), 7.27–7.35 (m, 2 H, ArH), 7.46 (d, J = 2.2 Hz, 1 H, ArH), 7.97 (d, J = 7.8 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 14.5, 16.4 (d, J_{CCOP} = 5.9 Hz), 16.6 (d, J_{CCOP} = 6.0 Hz), 41.6, 44.7 (d, J_{CP} = 208.0 Hz), 48.3 (d, J_{CCP} = 4.2 Hz), 63.0 (d, J_{COP} = 6.1 Hz), 63.7 (d, J_{COP} = 5.8 Hz), 63.8, 109.5, 121.1, 123.8, 126.8, 127.8, 128.8, 129.8, 130.5, 131.1, 133.8, 134.5, 143.8, 159.2, 170.1 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1741, 1723, 1243 cm^{-1}. HRMS: calcd. for $C_{23}H_{25}Cl_2N_2NaO_6P$ 549.0725; found 549.0722.

Ethyl 1′-Benzyl-3-(diethoxyphosphoryl)-2′-oxospiro[aziridine-2,3′-indoline]-1-carboxylate (3d): Yield: 151 mg (0.33 mmol, 33%); yellow solid; isolated as the *trans* isomer; R_f = 0.40 (hexane/ethyl acetate, 2:8). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.15 [t, J = 7.0 Hz, 3 H, (CH_3CH$_2$O)$_2$P], 1.23 [t, J = 7.0 Hz, 3 H, (CH_3CH$_2$O)$_2$P], 1.43 (t, J = 7.1 Hz, 3 H, CH_3CH$_2$OC), 3.40 (d, $J_{H,P}$ = 17.3 Hz, 1 H, NCH), 3.92–4.12 [m, 2 H, (CH$_3$CH_2O)$_2$P], 4.22 (q, J = 7.1 Hz, 2 H, CH$_3$CH_2O), 4.27–4.45 [m, 2 H, (CH$_3$CH_2O)$_2$P], 4.82 (d, J = 15.9 Hz, 1 H, NCH$_a$$H_b$), 5.14 (d, J = 15.8 Hz, 1 H, NCH_aH$_b$), 6.77 (d, J = 7.7 Hz, 1 H, ArH), 7.08 (t, J = 7.5 Hz, 1 H, ArH), 7.20–7.49 (m, 6 H, ArH), 7.93 (d, J = 7.6 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 14.4, 16.4 (d, J_{CCOP} = 5.9 Hz), 16.7 (d, J_{CCOP} = 6.0 Hz), 44.5 (d, J_{CP} = 207.5 Hz), 44.6, 48.4 (d, J_{CCP} = 4.1 Hz), 63.0 (d, J_{COP} = 6.2 Hz), 63.8 (d, J_{COP} = 5.7 Hz), 63.8, 109.8, 121.1, 123.4, 126.6, 127.3, 128.0, 129.1, 130.3, 135.2, 144.4, 159.6, 169.9 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1740, 1721, 1253 cm^{-1}. HRMS: calcd. for $C_{23}H_{27}N_2NaO_6P$ 481.1504; found 481.1500.

Ethyl 1′-Benzyl-3-(diethoxyphosphoryl)-5′-methoxy-2′-oxospiro[aziridine-2,3′-indoline]-1-carboxylate (3e): Yield: 157 mg (0.32 mmol, 32%); yellow solid; isolated as the *trans* isomer; R_f = 0.42 (hexane/ethyl acetate, 2:8). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.14 [t, J = 7.1 Hz, 3 H, (CH_3CH$_2$O)$_2$P], 1.21 [t, J = 7.2 Hz, 3 H, (CH_3CH$_2$O)$_2$P], 1.43 (t, J = 7.1 Hz, 3 H, CH_3CH$_2$OC), 3.38 (d, $J_{H,P}$ = 17.2 Hz, 1 H, NCH), 3.74 (s, 3 H, CH_3O), 3.90–4.10 [m, 2 H, (CH$_3$CH_2O)$_2$P], 4.20 (q, J = 7.1 Hz, 2 H, CH$_3$CH_2O), 4.29–4.44 [m, 2 H, (CH$_3$CH_2O)$_2$P], 4.76 (d, J = 15.8 Hz, 1 H, NCH$_a$$H_b$), 5.11 (d, J = 15.8 Hz, 1 H, NCH_aH$_b$), 6.64 (d, J = 8.6 Hz, 1 H, ArH), 6.75–6.80 (m, 1 H, ArH), 7.22–7.36 (m, 5 H, ArH), 7.65 (d, J = 2.6 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 14.4, 16.4 (d, J_{CCOP} = 5.9 Hz), 16.6 (d, J_{CCOP} = 6.0 Hz), 44.4 (d, J_{CP} = 207.7 Hz), 44.6, 48.6 (d, J_{CCP} = 4.1 Hz), 56.0, 63.0 (d, J_{COP} = 5.7 Hz), 63.8 (d, J_{COP} = 5.7 Hz), 63.8, 110.5, 112.2, 116.6, 122.2, 127.2, 128.0, 129.0, 135.3, 137.6, 156.4, 159.5, 169.6 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1740, 1719, 1257 cm^{-1}. HRMS: calcd. for $C_{24}H_{29}N_2NaO_7P$ 511.1610; found 511.1607.

Ethyl 1′-Benzyl-3-(diethoxyphosphoryl)-5′-isopropyl-2′-oxospiro[aziridine-2,3′-indoline]-1-carboxylate (3f): Yield: 240 mg (0.48 mmol, 48%); yellow solid; isolated as the *trans* isomer; R_f = 0.43 (hexane/ethyl acetate, 2:8). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.11 [t, J = 7.1 Hz, 3 H, (CH_3CH$_2$O)$_2$P], 1.16–1.29 [m, 9 H, (CH_3CH$_2$O)$_2$P, (CH_3)CH], 1.43 (t, J = 7.0 Hz, 3 H, CH_3CH$_2$OC), 2.87 [sept, J = 6.6 Hz, 1 H, (CH$_3$)CH], 3.38 (d, $J_{H,P}$ = 17.3 Hz, 1 H, NCH), 3.90–4.11 [m, 2 H, (CH$_3$CH_2O)$_2$P], 4.22 (q, J = 7.0 Hz, 2 H, CH$_3$CH_2O), 4.28–4.47 [m, 2 H, (CH$_3$CH_2O)$_2$P], 4.81 (d, J = 15.7 Hz, 1 H, NCH$_a$$H_b$), 5.09 (d, J = 15.7 Hz, 1 H, NCH_aH$_b$), 6.69 (d, J = 8.1 Hz, 1 H, ArH), 7.07–7.16 (m, 1 H, ArH), 7.21–7.44 (m, 5 H, ArH), 7.84–7.91 (m, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 14.4, 16.4 (d, J_{CCOP} = 5.9 Hz), 16.6 (d, J_{CCOP} = 6.0 Hz), 24.1, 24.4, 34.1, 44.5 (d, J_{CP} = 207.7 Hz), 44.6, 48.4, 62.9 (d, J_{COP} = 6.1 Hz), 63.6 (d, J_{COP} = 5.7 Hz), 63.7, 109.5, 121.1, 124.8, 127.3, 128.0, 128.1, 129.0, 135.4, 142.2, 144.3, 159.3, 169.9 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1737, 1720, 1251 cm^{-1}. HRMS: calcd. for $C_{26}H_{33}N_2NaO_6P$ 523.1974; found 523.1969.

General Procedure for Nucleophilic Epoxidation: In a round-bottomed flask was placed a solution of **4** (1 mmol, 1 M in EtOH) and 30% aqueous hydrogen peroxide (3 mmol, 0.34 mL). After cooling with an ice bath to 15 °C, aqueous sodium hydroxide (2 M, 0.125 mL, 0.25 mmol) was slowly added whilst stirring. The resulting mixture was stirred at 20–25 °C until the reaction was complete (TLC) and subsequently poured into saturated aqueous NH_4Cl solution (1.0 mL). The aqueous phase was extracted several times with EtOAc, and the combined organic phases were washed with brine, dried with anhydrous Na_2SO_4 and concentrated under reduced pressure to give the crude product, which was purified by flash chromatography on silica gel (hexane/ethyl acetate).

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Diethyl *trans*-1-Methyl-2-oxospiro[indoline-3,2′-oxiran]-3′-ylphosphonate (*trans*-4a): Yield: 218 mg (0.70 mmol, 70%); pale-yellow solid; R_f = 0.33 (hexane/ethyl acetate, 3:7). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.21 [t, J = 7.0 Hz, 3 H, ($CH_3CH_2O)_2P$], 1.41 [t, J = 7.1 Hz, 3 H, ($CH_3CH_2O)_2P$], 3.26 (s, 3 H, NCH_3), 3.73 (d, $J_{H,P}$ = 27.6 Hz, 1 H, OCH), 3.95–4.14 [m, 2 H, ($CH_3CH_2O)_2P$], 4.20–4.37 [m, 2 H, ($CH_3CH_2O)_2P$], 6.90 (d, J = 7.9 Hz, 1 H, ArH), 7.1 (dt, J = 7.7, 1.0 Hz, 1 H, ArH), 7.39 (dt, J = 7.9, 1.3 Hz, 1 H, ArH), 7.99 (d, J = 7.7 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 15.9 (d, J_{CCOP} = 5.8 Hz), 16.0 (d, J_{CCOP} = 5.7 Hz), 26.3, 55.5 (d, J_{CP} = 203.5 Hz), 59.7, 62.7 (d, J_{COP} = 6.3 Hz), 63.1 (d, J_{COP} = 6.1 Hz), 108.4, 118.9, 122.6, 126.5, 130.6, 145.3, 170.2 ppm. ^{31}P NMR: δ = 14.5 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1725, 1236 cm^{-1}. HRMS: calcd. for $C_{14}H_{18}NNaO_5P$ 334.0820; found 334.0816.

Diethyl *cis*-1-Methyl-2-oxospiro[indoline-3,2′-oxiran]-3′-ylphosphonate (*cis*-4a): Yield: 30 mg (0.10 mmol, 10%); pale-yellow solid; R_f = 0.23 (hexane/ethyl acetate, 3:7). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.35–1.43 [m, 6 H, ($CH_3CH_2O)_2P$], 3.26 (s, 3 H, NCH_3), 3.71 (d, $J_{H,P}$ = 27.4 Hz, 1 H, OCH), 4.18–4.48 [m, 4 H, ($CH_3CH_2O)_2P$], 6.89 (d, J = 7.9 Hz, 1 H, ArH), 7.04–7.08 (m, 2 H, ArH), 7.35–7.44 (m, 1 H, ArH) ppm.

Diethyl *trans*-2-Oxo-1-phenylspiro[indoline-3,2′-oxiran]-3′-ylphosphonate (*trans*-4b): Yield: 233 mg (0.62 mmol, 62%); yellow solid; R_f = 0.42 (hexane/ethyl acetate, 3:7). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.18 [t, J = 7.1 Hz, 3 H, ($CH_3CH_2O)_2P$], 1.34 [t, J = 7.1 Hz, 3 H, ($CH_3CH_2O)_2P$], 3.76 (d, $J_{H,P}$ = 27.6 Hz, 1 H, OCH), 4.00–4.08 [m, 2 H, ($CH_3CH_2O)_2P$], 4.18–4.33 [m, 2 H, ($CH_3CH_2O)_2P$], 6.77 (d, J = 7.6 Hz, 1 H, ArH), 7.05 (t, J = 7.6 Hz, 1 H, ArH), 7.22 (t, J = 7.6 Hz, 1 H, ArH), 7.35–7.46 (m, 5 H, ArH), 7.96 (d, J = 7.6 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 16.0 (d, J_{CCOP} = 5.7 Hz), 16.2 (d, J_{CCOP} = 5.8 Hz), 58.1 (d, J_{CP} = 203.7 Hz), 60.1, 62.9 (d, J_{COP} = 6.2 Hz), 63.4 (d, J_{COP} = 6.1 Hz), 109.8, 118.8, 123.3, 126.1, 126.9, 128.3, 129.5, 130.6, 133.5, 145.5, 169.8 ppm. ^{31}P NMR: δ = 14.4 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1716, 1265 cm^{-1}. HRMS: calcd. for $C_{19}H_{20}NNaO_5P$ 396.0977; found 396.0973.

Diethyl *cis*-2-Oxo-1-phenylspiro[indoline-3,2′-oxiran]-3′-ylphosphonate (*cis*-4b): Yield: 58 mg (0.16 mmol, 16%); yellow solid; R_f = 0.29 (hexane/ethyl acetate, 3:7). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.33–1.42 [m, 6 H, ($CH_3CH_2O)_2P$], 3.79 (d, $J_{H,P}$ = 27.3 Hz, 1 H, OCH), 4.18–4.45 [m, 4 H, ($CH_3CH_2O)_2P$], 6.86 (d, J = 7.9 Hz, 1 H, ArH), 7.05–7.14 (m, 2 H, ArH), 7.28–7.39 (m, 1 H, ArH), 7.40–7.57 (m, 5 H, ArH) ppm.

Diethyl *trans*-1-(2,4-Dichlorobenzyl)-2-oxospiro[indoline-3,2′-oxiran]-3′-ylphosphonate (*trans*-4c): Yield: 307 mg (0.67 mmol, 67%); yellow solid; R_f = 0.39 (hexane/ethyl acetate, 3:7). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.23 [t, J = 7.1 Hz, 3 H, ($CH_3CH_2O)_2P$], 1.42 [t, J = 7.1 Hz, 3 H, ($CH_3CH_2O)_2P$], 3.81 (d, $J_{H,P}$ = 27.4 Hz, 1 H, OCH), 3.97–4.19 [m, 2 H, ($CH_3CH_2O)_2P$], 4.22–4.39 [m, 2 H, ($CH_3CH_2O)_2P$], 5.03 (s, 2 H, CH_2N), 6.73 (d, J = 7.9 Hz, 1 H, ArH), 7.05–7.20 (m, 3 H, ArH), 7.30–7.34 (m, 3 H, ArH), 7.43 (d, J = 1.9 Hz, 1 H, ArH), 8.00 (d, J = 7.6 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 15.9 (d, J_{CCOP} = 5.6 Hz), 16.0 (d, J_{CCOP} = 5.5 Hz), 41.1, 57.9 (d, J_{CP} = 203.0 Hz), 59.7 (d, J_{CCP} = 1.1 Hz), 62.6 (d, J_{COP} = 6.2 Hz), 63.1 (d, J_{COP} = 6.2 Hz), 109.2, 118.9, 123.0, 126.8, 127.2, 128.8, 129.2, 130.6, 130.8, 133.2, 133.8, 144.0, 170.6 ppm. ^{31}P NMR: δ = 14.2 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1733, 1253 cm^{-1}. HRMS: calcd. for $C_{20}H_{20}C_{l2}NNaO_5P$ 478.0354; found 478.0350.

Diethyl *cis*-1-(2,4-Dichlorobenzyl)-2-oxospiro[indoline-3,2′-oxiran]-3′-ylphosphonate (*cis*-4c): Yield: 103 mg (0.22 mmol, 22%); yellow solid; R_f = 0.25 (hexane/ethyl acetate, 3:7). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.50 [t, J = 7.1 Hz, 6 H, ($CH_3CH_2O)_2P$], 3.87 (d, $J_{H,P}$ = 27.5 Hz, 1 H, OCH), 4.21–4.57 [m, 4 H, ($CH_3CH_2O)_2P$], 5.15 (s, 2 H, CH_2N), 6.83 (d, J = 7.3 Hz, 1 H, ArH), 7.14–7.52 (m, 6 H, ArH) ppm.

Diethyl *trans*-1-Benzyl-2-oxospiro[indoline-3,2′-oxiran]-3′-ylphosphonate (*trans*-4d): Yield: 263 mg (0.68 mmol, 68%); yellow solid; R_f = 0.41 (hexane/ethyl acetate, 3:7). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.22 [t, J = 7.1 Hz, 3 H, ($CH_3CH_2O)_2P$], 1.43 [t, J = 7.1 Hz, 3 H, ($CH_3CH_2O)_2P$], 3.81 (d, $J_{H,P}$ = 27.4 Hz, 1 H, OCH), 4.02–4.14 [m, 2 H, ($CH_3CH_2O)_2P$], 4.24–4.39 [m, 2 H, ($CH_3CH_2O)_2P$], 4.96 (s, 2 H, CH_2N), 6.81 (d, J = 7.6 Hz, 1 H, ArH), 7.07 (t, J = 7.6 Hz, 1 H, ArH), 7.24–7.36 (m, 6 H, ArH), 8.00 (d, J = 7.6 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 16.2 (d, J_{CCOP} = 5.7 Hz), 16.4 (d, J_{CCOP} = 5.8 Hz),44.4, 58.1 (d, J_{CP} = 203.1 Hz), 60.2 (d, J_{CCP} = 1.1 Hz), 62.9 (d, J_{COP} = 6.0 Hz), 63.3 (d, J_{COP} = 6.0 Hz), 109.3, 119.2, 122.1, 127.3, 127.5, 127.7, 128.7, 131.7, 135.2, 145.5, 170.7 ppm. ^{31}P NMR: δ = 14.4 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1731, 1262 cm^{-1}. HRMS: calcd. for $C_{20}H_{22}NNaO_5P$ 410.1133; found 410.1129.

Diethyl *cis*-1-Benzyl-2-oxospiro[indoline-3,2′-oxiran]-3′-ylphosphonate (*cis*-4d): Yield: 46 mg (0.12 mmol, 12%); yellow solid; R_f = 0.27 (hexane/ethyl acetate, 3:7). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.33 [t, J = 7.1 Hz, 6 H, ($CH_3CH_2O)_2P$], 3.69 (d, $J_{H,P}$ = 27.6 Hz, 1 H, OCH), 4.14–4.40 [m, 4 H, ($CH_3CH_2O)_2P$], 4.90 (s, 2 H, CH_2N), 6.71 (d, J = 7.8 Hz, 1 H, ArH), 6.92–7.02 (m, 2 H, ArH), 7.16–7.30 (m, 6 H, ArH) ppm.

Diethyl *trans*-1-Benzyl-5-methoxy-2-oxospiro[indoline-3,2′-oxiran]-3′-ylphosphonate (*trans*-4e): Yield: 333 mg (0.80 mmol, 80%); yellow solid; R_f = 0.40 (hexane/ethyl acetate, 3:7). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.23 [t, J = 7.1 Hz, 3 H, ($CH_3CH_2O)_2P$], 1.43 [t, J = 7.1 Hz, 3 H, ($CH_3CH_2O)_2P$], 3.77 (s, 3 H, OCH_3), 3.82 (d, $J_{H,P}$ = 27.4 Hz, 1 H, OCH), 3.97–4.17 [m, 2 H, ($CH_3CH_2O)_2P$], 4.24–4.41 [m, 2 H, ($CH_3CH_2O)_2P$], 4.93 (s, 2 H, CH_2N), 6.68 (d, J = 8.6 Hz, 1 H, ArH), 6.79–6.85 (m, 1 H, ArH), 7.27–7.40 (m, 5 H, ArH), 7.74 (d, J = 2.6 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 16.2 (d, J_{CCOP} = 6.4 Hz), 16.4 (d, J_{CCOP} = 6.8 Hz), 44.5, 55.8, 58.0 (d, J_{CP} = 189.5 Hz), 60.3 (J_{CCP} = 1.1 Hz), 63.0 (d, J_{COP} = 5.8 Hz), 63.5 (d, J_{COP} = 5.7 Hz), 110.3, 112.8, 116.9, 120.4, 127.3, 127.8, 128.8, 135.1, 138.0, 156.1, 170.6 ppm. ^{31}P NMR: δ = 14.7 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1728, 1240 cm^{-1}. HRMS: calcd. for $C_{21}H_{24}NNaO_6P$ 440.1239; found 440.1236.

Diethyl *cis*-1-Benzyl-5-methoxy-2-oxospiro[indoline-3,2′-oxiran]-3′-ylphosphonate (*cis*-4e): Yield: 68 mg (0.16 mmol, 16%); yellow solid; R_f = 0.22 (hexane/ethyl acetate, 3:7). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.39 [t, J = 7.1 Hz, 6 H, ($CH_3CH_2O)_2P$], 3.71 (d, $J_{H,P}$ = 27.5 Hz, 1 H, OCH), 3.73 (s, 3 H, OCH_3), 4.07–4.44 [m, 4 H, ($CH_3CH_2O)_2P$], 4.93 (s, 2 H, CH_2N), 6.62–6.69 (m, 2 H, ArH), 6.75–6.82 (m, 1 H, ArH), 7.27–7.34 (m, 5 H, ArH) ppm.

Diethyl *trans*-1-Benzyl-5-isopropyl-2-oxospiro[indoline-3,2′-oxiran]-3′-ylphosphonate (*trans*-4f): Yield: 365 mg (0.85 mmol, 85%); yellow solid; R_f = 0.42 (hexane/ethyl acetate, 3:7). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.17–1.29 [m, 9 H, ($CH_3CH_2O)_2P$, (CH_3)-CH], 1.42 [t, J = 7.1 Hz, 3 H, ($CH_3CH_2O)_2P$], 2.87 [sept, J = 6.6 Hz, 1 H, (CH_3)C*H*], 3.80 (d, $J_{H,P}$ = 27.7 Hz, 1 H, OCH), 4.00–4.17 [m, 2 H, ($CH_3CH_2O)_2P$], 4.24–4.41 [m, 2 H, ($CH_3CH_2O)_2P$], 4.93 (s, 2 H, CH_2N), 6.71 (d, J = 7.9 Hz, 1 H, ArH), 7.13 (d, J = 7.9 Hz, 1 H, ArH), 7.29–7.42 (m, 5 H, ArH), 7.35 (d, J = 1.1 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 16.1 (d, J_{CCOP} = 5.7 Hz), 16.3 (d, J_{CCOP} = 5.7 Hz), 23.9, 24.0, 33.8, 44.4, 58.1 (d, J_{CP} = 203.1 Hz), 60.2 (d, J_{CCP} = 1.0 Hz), 62.9 (d, J_{COP} = 6.1 Hz), 63.2 (d, J_{COP} = 6.1 Hz), 109.3, 119.3, 125.2, 127.3, 127.7,

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128.6, 128.7, 135.2, 142.6, 143.9, 170.8 ppm. ^{31}P NMR: δ = 14.9 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1731, 1236 cm^{-1}. HRMS: calcd. for $C_{23}H_{28}NNaO_5P$ 452.1603; found 452.1600.

Diethyl *cis*-1-Benzyl-5-isopropyl-2-oxospiro[indoline-3,2′-oxiran]-3′-ylphosphonate (*cis*-4f): Yield: 30 mg (0.07 mmol, 7%); yellow solid; R_f = 0.24 (hexane/ethyl acetate, 3:7). ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.17 [d, J = 6.8 Hz, 6 H, (CH_3)CH], 1.36 [t, J = 7.0 Hz, 6 H, ($CH_3CH_2O)_2$P], 2.83 [sept, J = 6.8 Hz, 1 H, (CH_3)C*H*], 3.74 (d, $J_{H,P}$ = 27.8 Hz, 1 H, OCH), 4.20–4.44 [m, 4 H, ($CH_3CH_2O)_2$P], 4.94 (s, 2 H, CH_2N), 6.78 (d, J = 8.1 Hz, 1 H, ArH), 6.92 (d, J = 1.6 Hz, 1 H, ArH), 7.11 (d, J = 8.1 Hz, 1 H, ArH), 7.29–7.43 (m, 5 H, ArH) ppm.

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