

# Synthesis of Optically Pure Highly Functionalized $\gamma$ -Lactams via 2-Azetidinone-Tethered Iminophosphoranes

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**Abstract:** A synthesis of optically pure densely functionalized  $\gamma$ -lactams starting from 2-azetidinone-tethered iminophosphoranes has been developed. Full chirality transfer has been accomplished from the enantiomerically pure 2-azetidinones. The addition of lithium acetylides to 4-oxoazetidine-2-carbaldehydes at  $-78^\circ\text{C}$  smoothly yielded propargylic alcohols with excellent diastereoselectivities. Propargylic alcohols were converted to mesylates, which by exposure to sodium azide afforded the corresponding azides. Treatment of  $\beta$ -lactams bearing an azido side chain with triphenylphosphine (TPP) gave  $\lambda^5$ -phosphazenes (iminophosphoranes, phosphine imines), which were not isolated. The sodium methoxide promoted reaction of the phosphazene  $\beta$ -lactams smoothly provided  $\gamma$ -lactams, through a N1–C2 bond breakage process on the four-membered lactam with concomitant ring expansion, followed by hydrolysis.

Nitrogen heterocycles comprise the vast majority of medicinals on the market today. Highly substituted lactam rings possess diverse biological activity, and much recent attention has focused on excitatory amino acid chemistry, particularly as a result of the drive to better understand CNS function in mammalian systems.<sup>1</sup> It has recently also been shown that densely functionalized pyrrolidinones, such as lactacystin<sup>2</sup> and pramamicin,<sup>3</sup> exhibit potent and selective activity in proteasome inactivation and may find application in the development of selective therapeutic agents for important parasitic infections.<sup>4</sup> In addition, the pyrrolidinone ( $\gamma$ -lactam) functionality is a prevalent theme in various natural product syntheses, and serves as a crucial intermediate for numerous natural products. On the other hand, the importance of 2-azetidinones as synthetic intermediates has been widely recognized in organic synthesis. This usefulness is based on the impressive variety of transformations which can be derived from this system, because ring cleavage of any of the four single bonds of the  $\beta$ -lactam system is enhanced by ring strain. Selective bond cleavage of the 2-azetidinone ring coupled with

further interesting synthetic transformations renders these fascinating molecules powerful synthetic building blocks.<sup>5–7</sup> Despite the versatility of the 2-azetidinone ring,<sup>8</sup> synthetic routes to monocyclic  $\gamma$ -lactams from  $\beta$ -lactams have been scarcely reported.<sup>9</sup> We have used carbonyl  $\beta$ -lactams as chiral templates and recently shown their manipulation to a variety of potentially bioactive products.<sup>10</sup> In this paper we present a  $\beta$ -lactam-tethered iminophosphorane-based stereocontrolled access to enantiopure  $\gamma$ -lactams.

Starting substrates, enantiopure 4-oxoazetidine-2-carbaldehydes **1a–e**, were obtained as single cis-enantiomers from imines of (*R*)-2,3-*O*-isopropylidene-glyceraldehyde through Staudinger reaction with the appropriate alkoxyacetyl chloride in the presence of  $\text{Et}_3\text{N}$ , followed by sequential acidic acetone hydrolysis and oxidative cleavage.<sup>10</sup>

Coupling reactions of alkynes (and alkynylmetallic reagents) and aldehydes are important transformations in organic synthesis as they generate new carbon–carbon bonds to give propargyl alcohols. Optically active propargylic alcohols serve as versatile building blocks for asymmetric synthesis, as they are used in diverse areas, including the synthesis of natural products, pharmaceuticals, and macromolecules.<sup>11</sup> Our interest in the use of 4-oxoazetidine-2-carbaldehydes as substrates for addition reactions<sup>10</sup> prompted us to evaluate their alkynylation reaction with acetylenes. We found particularly attractive the catalytic activation of the alkyne and subsequent addition to the carbonyl derivative. However, neither the Knochel procedure with cesium hydroxide<sup>12</sup> nor the Carreira protocol with zinc triflate/*N*-methylephedrine<sup>13</sup> were amenable to our  $\beta$ -lactam aldehydes. Aldehydes **1**

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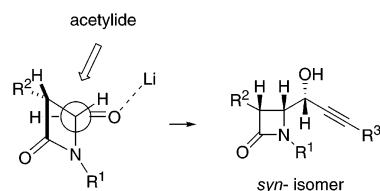
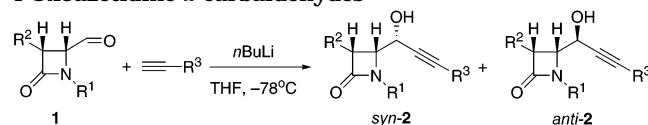


FIGURE 1.

were almost unreactive under catalytic Carreira's conditions, while epimerization was observed on the  $\alpha$ -amino aldehyde for the cesium hydroxide-catalyzed reaction.<sup>14</sup> Next, we focused our efforts on the alkynylation of aldehydes **1** using equimolecular amounts of Lewis acid in combination with a tertiary amine.<sup>15</sup> Despite the claimed mildness of the procedure promoted by zinc(II) salts in the presence of triethylamine,<sup>16</sup> it was also unfeasible for  $\alpha$ -amino aldehydes **1** because it caused the undesired side epimerization reaction. Then, we turned our attention to the classical use of a stoichiometric amount of base, such as an organolithium reagent, to generate a metal acetylide. Thus, the addition of lithium(trimethylsilyl)acetylide or lithium(phenyl)acetylide to 4-oxazetidine-2-carbaldehydes **1a–e** in THF at  $-78^\circ\text{C}$  smoothly yielded the propargylic alcohols **2a–i**. Importantly, the  $\beta$ -lactam ring stereochemistry was unaffected by this process.<sup>17</sup> Total diastereoselectivity was generally observed when different aldehydes were used (Table 1, entries 1–7). However, aldehyde (+)-**1e** bearing a methoxy substituent at C3 and a 3-butenyl moiety at N1 provided poor diastereoselectivity (70:30) with the same facial preference (Table 1, entries 8 and 9). The bulkiness of the phenoxy substituent at C3 or the *p*-methoxyphenyl at N1 on the  $\beta$ -lactam ring may play a role in ensuring the high selectivity of this process, while less demanding groups dropped the diastereoselectivity. The observed syn-diastereoselectivity might be tentatively explained by invoking the Felkin–Anh model (Figure 1) analogously to related addition processes described in our laboratories.<sup>8a</sup>

Organic azides are extremely valuable intermediates for the synthesis of many nitrogen-containing molecules, including heterocycles and natural products. Our next target was the synthesis of 2-azetidinone-tethered azides, because they bear the azido moiety that serves as a latent amine. The direct conversion of alkynols **2** into the corresponding azides failed with different reagents such as  $\text{NaN}_3/\text{BF}_3\cdot\text{Et}_2\text{O}$  or DPPA/DBU.<sup>18</sup> Then, propargylic alcohols **2** were converted to mesylates **3** by exposure to

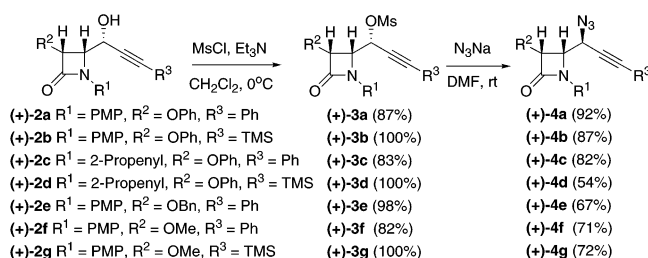
TABLE 1. Stereoselective Alkynylation of 4-Oxazetidine-2-carbaldehydes



entry	aldehyde	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	alkynol	syn/anti ratio <sup>a</sup>	yield (%) <sup>b</sup>
1	(+)- <b>1a</b>	PMP <sup>c</sup>	PhO	Ph	(+)- <b>2a</b>	100:0	79
2	(+)- <b>1a</b>	PMP	PhO	TMS <sup>d</sup>	(+)- <b>2b</b>	100:0	81
3	(+)- <b>1b</b>	2-propenyl	PhO	Ph	(+)- <b>2c</b>	100:0	66
4	(+)- <b>1b</b>	2-propenyl	PhO	TMS	(+)- <b>2d</b>	100:0	70
5	(+)- <b>1c</b>	PMP	BnO	Ph	(+)- <b>2e</b>	100:0	77
6	(+)- <b>1d</b>	PMP	MeO	Ph	(+)- <b>2f</b>	100:0	64
7	(+)- <b>1d</b>	PMP	MeO	TMS	(+)- <b>2g</b>	100:0	56
8	(+)- <b>1e</b>	3-butenyl	MeO	Ph	(+)- <b>2h</b>	70:30	54
9	(+)- <b>1e</b>	3-butenyl	MeO	TMS	(+)- <b>2i</b>	70:30	42

<sup>a</sup> The ratio was determined by integration of well-resolved signals in the  $^1\text{H}$  NMR spectra of the crude reaction mixtures before purification. <sup>b</sup> Yield of pure, isolated product with correct analytical and spectral data. <sup>c</sup> PMP = 4-MeOC<sub>6</sub>H<sub>4</sub>. <sup>d</sup> TMS = trimethylsilyl.

SCHEME 1



methanesulfonyl chloride and triethylamine. Mesylates **3** were transformed into azides **4** when treated with  $\text{NaN}_3$  (Scheme 1). Optimum conditions for the reaction have been explored and the reaction was found to proceed smoothly to completion with use of 3 molar equiv of  $\text{NaN}_3$  in DMF at room temperature overnight.

Formation of iminophosphoranes is a convenient way of generating nucleophilic amines from organic azides. It was found that the phosphine imine intermediates **5a–g** were formed satisfactorily (we used IR spectroscopy to follow the disappearance of the azide absorption at about  $2100\text{ cm}^{-1}$ ) by reaction of azides **4** with triphenylphosphine (Scheme 2).<sup>19</sup> Initially, we tried to reduce azide (+)-**4b** to amine (+)-**6a** using the triphenylphosphine method, but hydrolysis of the iminophosphorane was slow and the isolated yield of amine (+)-**6a** was very poor (25%) (Scheme 3). Although complete conversion was observed by TLC and  $^1\text{H}$  NMR analysis of the crude reaction mixture, the high polarity of amine **6a** and subsequent high water solubility may be responsible for the modest isolated yield in the aqueous reaction media.

Studies by Vilarrosa and co-workers have shown that the phosphazene intermediate can be coupled to acids,

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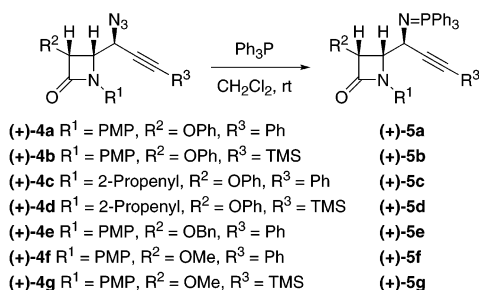
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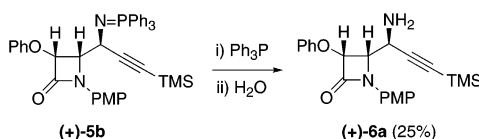
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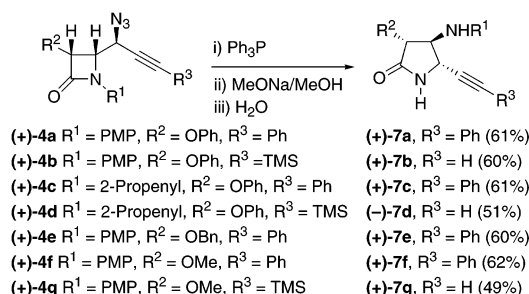
## SCHEME 2



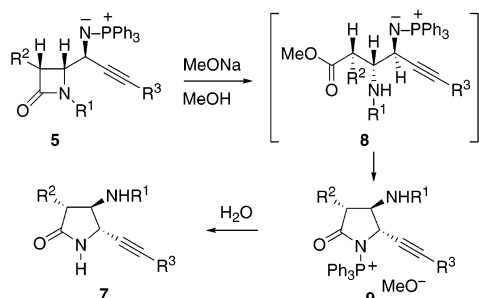
## SCHEME 3



## SCHEME 4



## SCHEME 5



acid halides, or acid anhydrides to yield an amide in a straightforward manner.<sup>20</sup> It occurred to us that the Staudinger protocol might serve as a novel one-pot flask procedure for the direct conversion of 2-azetidinone-tethered azides into  $\gamma$ -lactams. Indeed, the sequential treatment of  $\beta$ -lactam azides **4** under meticulously dry conditions with triphenylphosphine and sodium methoxide, followed by an aqueous workup yielded the enantiopure pyrrolidinones **7** in reasonable yields (Scheme 4). When applicable, the trimethylsilyl protecting group was cleaved under the reaction conditions.

From a mechanistic point of view, our results could be explained through a bond breakage process on the four-

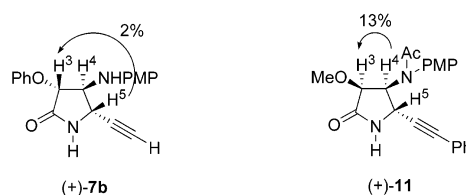
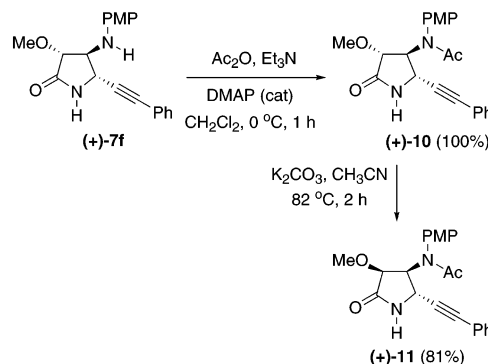


FIGURE 2.

## SCHEME 6



membered lactam with concomitant ring expansion, followed by hydrolysis. Initially, the selective N1–C2 bond cleavage of the  $\beta$ -lactam nucleus in 2-azetidinone-tethered iminophosphoranes **5** gave the nonisolable  $\beta$ -amino- $\gamma$ -phosphine imino esters **8**, which after rearrangement under the reaction conditions followed by hydrolysis of the phosphonium salts **9** yielded the  $\gamma$ -lactams **7** (Scheme 5). The pyrrolidinone formation must be driven by relief of the strain associated with the four-membered ring on forming a more stable five-membered ring. Azacycles **7** showed a single set of signals in their <sup>1</sup>H NMR spectra, thus proving that this transformation proceeded without detectable epimerization.

To show the capacity of the method to prepare an array of  $\gamma$ -lactams bearing stereochemical diversity, the  $\alpha$ -proton of the lactam moiety in the 2-pyrrolidinone nucleus was regiospecifically epimerized at C3. Previously to the epimerization reaction, the exocyclic amino group on  $\gamma$ -lactam (+)-7f was acetylated to give (+)-10. The enantiomerically pure  $\gamma$ -lactam (+)-11 was obtained in 81% overall yield from (+)-7f after sequential treatment with acetic anhydride and potassium carbonate (Scheme 6).

The stereochemistry of  $\gamma$ -lactams **7** and **10** was established by NMR techniques, particularly by vicinal proton couplings and qualitative homonuclear NOE difference spectra. The *cis*-stereochemistry of the four-membered ring is set during the cyclization step to form the 2-azetidinone ring and it is transferred unaltered during the further synthetic steps.<sup>17</sup> Taking into account that  $\beta$ -lactams **4** could be obtained and cyclized, the stereochemistry at the exocyclic stereogenic center for compounds **2–6** was immediately deduced by comparison with the NOE results of the cyclic five-membered lactams **7** and **11**. For compound (+)-7b the only significant NOE enhancement (2%) was observed on H3 upon irradiation on H5. For compound (+)-11, NOE irradiation of H4 resulted in a 13% enhancement on H3, while no effect was observed for H5. Thus, an *anti,anti*-relative stereochemistry was assigned for compound (+)-7b, while a *syn,anti*-disposition was established for compound (+)-11 (Figure 2).

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In conclusion, treatment of  $\beta$ -lactams bearing an azido side chain with triphenylphosphine gave 2-azetidinone-tethered iminophosphoranes, which have been found to react smoothly with sodium methoxide providing enantiopure  $\gamma$ -lactams. The transformation of  $\beta$ -lactam phosphazenes into pyrrolidinones involves the amide bond cleavage of the  $\beta$ -lactam ring, followed by cyclization of the resulting  $\beta$ -amino- $\gamma$ -phosphine imino ester with concomitant ring expansion, followed by hydrolysis.

## Experimental Section

**General.** General experimental data and procedures have been previously reported.<sup>10</sup> NMR spectra were recorded in CDCl<sub>3</sub> solutions, except where otherwise stated. Chemical shifts are given in ppm relative to TMS (<sup>1</sup>H, 0.0 ppm), or CDCl<sub>3</sub> (<sup>13</sup>C, 77.0 ppm). All commercially available compounds were used without further purification.

**General Procedure for the Preparation of Propargylic Alcohols 2.** A cooled solution of BuLi (3.79 mL, 6.06 mmol, 1.6 M in hexanes) was added dropwise to a stirred solution of the appropriate acetylene (6.06 mmol) in THF (10 mL) at  $-78^{\circ}\text{C}$ . After 30 min, the resulting solution was transferred via cannula to a solution of the corresponding 4-oxoazetidine-2-carbaldehyde **1** (2.02 mmol) in THF (10 mL) cooled at  $-78^{\circ}\text{C}$ , and the mixture was stirred for 4 h at  $-78^{\circ}\text{C}$ . Saturated aqueous ammonium chloride (6 mL) was added and the mixture was allowed to warm to room temperature, before being extracted with ethyl acetate (3  $\times$  10 mL). The organic extract was washed with brine, dried (MgSO<sub>4</sub>), and concentrated under reduced pressure. Chromatography of the residue eluting with ethyl acetate/hexanes mixtures gave analytically pure compounds **2**. Spectroscopic and analytical data for some representative pure forms of **2** follow.<sup>21</sup>

**Propargylic Alcohol (+)-2b.** From 600 mg (2.02 mmol) of aldehyde (+)-**1a**, 644 mg (81%) of (+)-**2b** was obtained as a colorless oil. [ $\alpha$ ]<sub>D</sub> +72.0 (*c* 0.6, CHCl<sub>3</sub>). <sup>1</sup>H NMR  $\delta$  0.01 (s, 9H), 2.49 (d, 1H, *J* = 5.5 Hz), 3.81 (s, 3H), 4.66 (t, 1H, *J* = 4.9 Hz), 4.95 (t, 1H, *J* = 4.8 Hz), 5.40 (d, 1H, *J* = 4.9 Hz), 6.77 (m, 2H), 6.95 (m, 3H), 7.20 (m, 2H), 7.47 (m, 2H). <sup>13</sup>C NMR  $\delta$  163.8, 157.6, 156.8, 130.9, 129.0, 128.9, 127.9, 118.5, 118.3, 92.9, 89.7, 63.2, 59.8, 59.2, 58.0,  $-0.6$ . IR (CHCl<sub>3</sub>, cm<sup>-1</sup>)  $\nu$  3303, 1745. MS (CI), *m/z* 396 (*M*<sup>+</sup> + 1, 100), 395 (*M*<sup>+</sup>, 12). Anal. Calcd for C<sub>22</sub>H<sub>25</sub>NO<sub>4</sub>Si: C, 66.81; H, 6.37; N, 3.54. Found: C, 66.70; H, 6.33; N, 3.52.

**General Procedure for the Preparation of Propargylic Methanesulfonates 3.** Methanesulfonyl chloride (138 mg, 1.20 mmol) and triethylamine (243 mg, 2.40 mmol) were sequentially added dropwise to a stirred solution of the corresponding propargylic alcohol (1.0 mmol) in dichloromethane (10 mL) at  $0^{\circ}\text{C}$ , and the mixture was stirred for 1 h at room temperature. The organic phase was washed with water (2  $\times$  5 mL), dried (MgSO<sub>4</sub>), and concentrated under reduced pressure. Chromatography of the residue eluting with hexanes/ethyl acetate mixtures gave analytically pure methanesulfonates **3**. Spectroscopic and analytical data for some representative pure forms of **3** follow.

**Propargylic Methanesulfonate (+)-3b.** From 54 mg (0.137 mmol) of alcohol (+)-**2b**, 65 mg (100%) of compound (+)-**3b** was obtained as a colorless oil. [ $\alpha$ ]<sub>D</sub> +51.8 (*c* 0.7, CHCl<sub>3</sub>). <sup>1</sup>H NMR  $\delta$  0.00 (s, 9H), 2.75 (s, 3H), 3.69 (s, 3H), 4.65 (dd, 1H, *J* = 6.7, 5.1 Hz), 5.34 (d, 1H, *J* = 5.1 Hz), 5.50 (d, 1H, *J* = 6.7 Hz), 7.80 (m, 9H). <sup>13</sup>C NMR  $\delta$  162.9, 157.6, 157.6, 157.1, 129.8, 129.6, 122.8, 120.0, 116.0, 114.3, 97.6, 97.2, 79.7, 69.9, 59.4, 55.5, 39.1,  $-0.6$ . IR (CHCl<sub>3</sub>, cm<sup>-1</sup>)  $\nu$  1746, 1354. MS (EI), *m/z* 474 (*M*<sup>+</sup> + 1, 3), 473 (*M*<sup>+</sup>, 100). Anal. Calcd for C<sub>23</sub>H<sub>27</sub>NO<sub>6</sub>SSi: C, 58.33; H, 5.75; N, 2.96. Found: C, 58.44; H, 5.72; N, 2.94.

**General Procedure for the Preparation of Propargylic Azides 4.** A solution of the appropriate methanesulfonate **3** (1.0 mmol) in dimethylformamide (5 mL) was added to a stirred

solution of sodium azide (3.0 mmol) in dimethylformamide (15 mL) at room temperature. The mixture was stirred at room temperature overnight, and water (5 mL) was added before being extracted with ethyl acetate (3  $\times$  10 mL). The organic phase was washed with water (2  $\times$  5 mL), dried (MgSO<sub>4</sub>), and concentrated under reduced pressure. Chromatography of the residue eluting with hexanes/ethyl acetate mixtures gave analytically pure azides **4**. Spectroscopic and analytical data for some representative pure forms of **4** follow.

**Propargylic Azide (+)-4b.** From 127 mg (0.268 mmol) of methanesulfonate (+)-**3b**, 97 mg (87%) of compound (+)-**4b** was obtained as a yellow oil. [ $\alpha$ ]<sub>D</sub> +135.3 (*c* 0.8, CHCl<sub>3</sub>). <sup>1</sup>H NMR  $\delta$  0.02 (s, 9H), 3.75 (s, 3H), 4.48 (dd, 1H, *J* = 4.9, 4.1 Hz), 4.75 (d, 1H, *J* = 4.1 Hz), 5.38 (d, 1H, *J* = 5.1 Hz), 6.77 (m, 2H), 7.00 (m, 3H), 7.24 (m, 2H), 7.41 (m, 2H). <sup>13</sup>C NMR  $\delta$  162.8, 157.5, 156.9, 129.8, 129.6, 122.5, 119.8, 115.8, 114.3, 97.2, 95.5, 79.4, 59.8, 55.4, 52.1,  $-0.6$ . IR (CHCl<sub>3</sub>, cm<sup>-1</sup>)  $\nu$  2112, 1746. MS (CI), *m/z* 421 (*M*<sup>+</sup> + 1, 100), 420 (*M*<sup>+</sup>, 7). Anal. Calcd for C<sub>22</sub>H<sub>24</sub>N<sub>4</sub>O<sub>3</sub>Si: C, 62.83; H, 5.75; N, 13.32. Found: C, 62.90; H, 5.71; N, 13.36.

**General Procedure for the Preparation of  $\gamma$ -Lactams 7.** A solution of triphenylphosphine (0.76 mmol) in dichloromethane (4 mL) was added to a stirred solution of the appropriate azide **4** (0.76 mmol) in dichloromethane (7 mL) at  $0^{\circ}\text{C}$ , and the mixture was stirred at room temperature for 3 h. The dichloromethane was removed under reduced pressure and the resulting crude iminophosphoranes **5** were solved in anhydrous methanol (15 mL). Then, sodium methoxide (164 mg, 3.0 mmol) was added in portions at  $0^{\circ}\text{C}$  to the methanolic solution of the corresponding iminophosphorane **5** (0.76 mmol). The reaction was stirred at room temperature for 2 h and then water was added (1 mL). The methanol was concentrated under reduced pressure, the aqueous residue was extracted with ethyl acetate (4  $\times$  5 mL), the organic layer was dried over MgSO<sub>4</sub>, and the solvent was removed under reduced pressure. Chromatography of the residue eluting with ethyl acetate/hexanes mixtures gave analytically pure compounds **7**.

**$\gamma$ -Lactam (+)-7b.** From 20 mg (0.047 mmol) of azide (+)-**4b**, 15 mg (60%) of compound (+)-**7b** was obtained as a colorless oil. [ $\alpha$ ]<sub>D</sub> +12.9 (*c* 0.8, CHCl<sub>3</sub>). <sup>1</sup>H NMR  $\delta$  2.34 (d, 1H, *J* = 2.1 Hz), 3.58 (s, 3H), 4.02 (dd, 1H, *J* = 5.1, 2.1 Hz), 4.15 (m, 1H), 4.49 (d, 1H, *J* = 5.7 Hz), 5.96 (s, 1H), 6.52 (m, 4H), 6.80 (m, 3H), 7.05 (m, 2H). <sup>13</sup>C NMR  $\delta$  170.9, 157.9, 153.5, 139.1, 129.4, 122.3, 116.4, 116.1, 114.8, 80.3, 80.2, 63.7, 55.6, 48.4, 29.6. IR (CHCl<sub>3</sub>, cm<sup>-1</sup>)  $\nu$  3310, 1750. MS (CI), *m/z* 323 (*M*<sup>+</sup> + 1, 100), 322 (*M*<sup>+</sup>, 9). Anal. Calcd for C<sub>19</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub>: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.90; H, 5.60; N, 8.74.

**Procedure for the Preparation of  $\gamma$ -Lactam (+)-11.** A stirred suspension of the  $\gamma$ -lactam (+)-**10** (37 mg, 0.098 mmol) and potassium carbonate (135 mg, 0.98 mmol) in acetonitrile (2 mL) was heated at reflux temperature for 2 h. After cooling to room temperature, the solid was removed by filtration, and the filtrate was concentrated under reduced pressure. Chromatography of the residue with ethyl acetate gave 30 mg (81%) of analytically pure compound (+)-**11** as a yellow oil.

**$\gamma$ -Lactam (+)-11.** [ $\alpha$ ]<sub>D</sub> +32.7 (*c* 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR  $\delta$  2.49 (s, 3H), 3.59 (s, 3H), 3.69 (s, 3H), 4.17 (m, 1H), 4.20 (d, 1H, *J* = 5.7 Hz), 4.52 (d, 1H, *J* = 5.6 Hz), 6.57 (m, 2H), 6.74 (m, 2H), 7.33 (m, 5H). <sup>13</sup>C NMR  $\delta$  171.0, 170.3, 153.4, 139.1, 132.1, 129.1, 128.4, 128.3, 115.3, 114.7, 78.5, 59.3, 56.1, 55.8, 49.4, 25.1. IR (CHCl<sub>3</sub>, cm<sup>-1</sup>)  $\nu$  3306, 1748, 1652. MS (CI), *m/z* 379 (*M*<sup>+</sup> + 1, 100), 378 (*M*<sup>+</sup>, 17). Anal. Calcd for C<sub>22</sub>H<sub>22</sub>N<sub>2</sub>O<sub>4</sub>: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.92; H, 5.83; N, 7.36.

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**Supporting Information Available:** Spectroscopic and analytical data for isomerically pure compounds (+)-**2a**, (+)-**2c-i**, (+)-**3a**, (+)-**3c-g**, (+)-**4a**, (+)-**4c-g**, (+)-**6a**, (+)-**7a**, (+)-**7c-g**, and (+)-**10**, as well as experimental procedures for compounds (+)-**6** and (+)-**10**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(21) Full spectroscopic and analytical data for compounds not included in this Experimental Section are described in the Supporting Information.