# Stereoselective Synthesis of α-Alkylazetidinones by a Free Radical Chain Reaction

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With a chain reaction mediated by tributyltin radical, benzhydryl 6-bromo- or 6,6-dibromopenicillanate was converted stereoselectively to either the 6α-alkylpenicillanate **9** as the only diastereomer or to the 6β-alkylpenicillanate **11** as the major isomer. Similarly, the trans or cis 3-alkylazetidinones **13** and **14** were obtained stereoselectively from the 3,3-dibromo precursor **12**.

## Introduction

The discovery of thienamycin (**1**) as a β-lactam antibiotic has revolutionized the accepted structure–activity concept with respect to configuration around the azetidinone ring and the nature of the side chain of the azetidinone moiety. The introduction of an analogue of **1** as a medicinal agent has led to renewed interest in the modification of earlier antibiotics such as penicillins **2** and cephalosporins **3** at the 6- and 7-positions, respectively[1,2] (Scheme I).

Metalation of both the 6-halopenicillanates and 7-halocephalosporanates have been used to introduce nonamidic side chains, albeit resulting in diastereomers.[3] The widespread use of electrophilic olefins to trap organic radicals generated from alkyl halides by a free radical chain mechanism[4] prompted us to investigate the suitability of 6-bromo- or 6,6-dibromopenicillanates as precursors for such trapping experiments.

## Results and Discussion

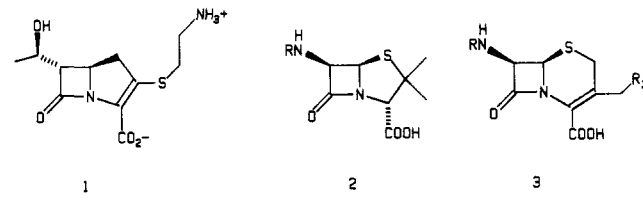
The 6α-bromo and 6,6-dibromopenicillanic acids were prepared from 6α-aminopenicillanic acid (6-APA) by known methods[5,6] and transformed to their benzhydryl esters **4** and **5** respectively in good yields. Reduction of the dibromopenicillin **5** with equimolar amount of tributyltin hydride gave 6β-bromopenicillanate **6** as the only diastereomer together with the reduction product **7** (Scheme II). This latter type of reaction was well investigated by Manhas et al.,[7] who proposed that the radical intermediate formed at C-6 abstracted the proton from the bulky tributyltin hydride from the less hindered side of the azetidinone, giving the cis-bromo isomer.

Reaction of either the *cis*- or *trans*-6-bromopenicillanate **6** or **4** and the excess olefin **8** with slow addition of tributyltin hydride, gave 30–35% reduction product **7** and 40–67% of the trans penicillinate **9** (method A, Table I).

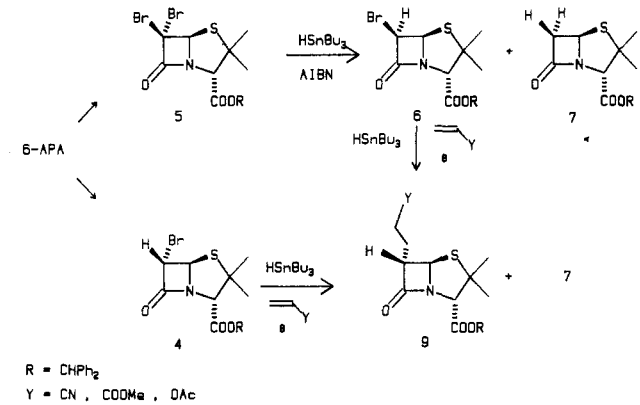
The 6,6-dibromopenicillanate **5** can be directly transformed to the trans product **9** by a one-pot procedure by first refluxing a solution of **5** with tributyltin hydride (1 equiv) followed by addition of the olefin (15–20 equiv) and slow addition of tributyltin hydride, giving similar overall yields (method B).

Alternatively, reacting the 6,6-dibromopenicillanate **5** with excess olefin **8** and tributyltin hydride (1 equiv) followed by removal of the excess olefin **8** and treatment of the residue with tributyltin hydride gave 40–55% reduction product **7** and 35–47% of the cis penicillanate **11** as the major diastereomer (method C) (Scheme III).

**Scheme I**



**Scheme II**



**Scheme III**

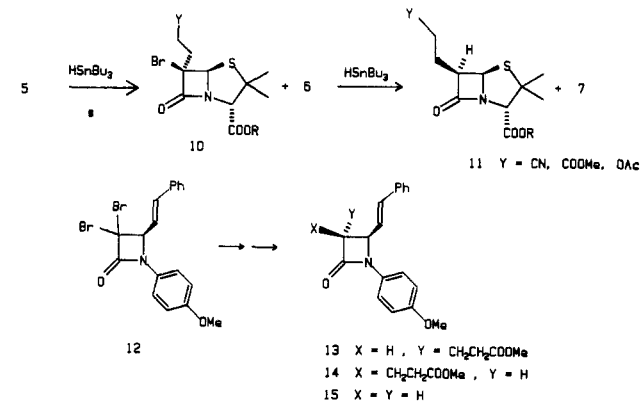


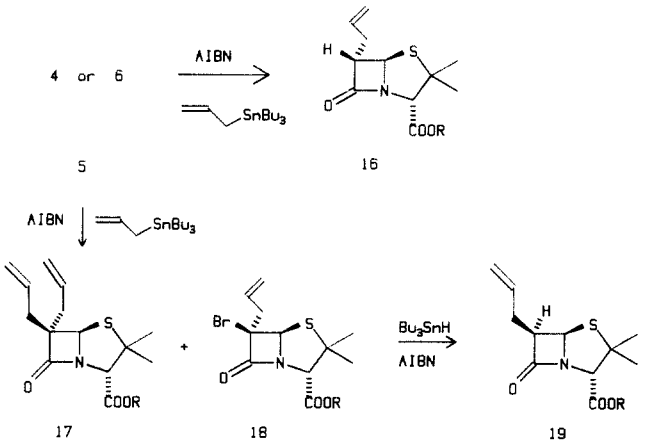
**Table I. Reaction of Bromopenicillinates with Olefins 8**

| entry | substrate | 8, Y | method | yield, % *trans*-9 | yield, % *cis*-11 |
|---|---|---|---|---|---|
| **a** | 4 | CN | A | 67 | |
| **b** | 5 | CN | B | 48 | |
| **c** | 5 | CN | C | 8 | 47 |
| **d** | 4 | COOMe | A | 55 | |
| **e** | 5 | COOMe | C | 6 | 44 |
| **f** | 4 | OAc | A | 43 | |
| **g** | 5 | OAc | C | 5 | 35 |

(1) Sheehan, J. C.; Lo, Y. S. *J. Org. Chem.* **1973**, *28*, 3227.
(2) Sheehan, J. C.; Buku, A.; Chocko, E.; Commons, T. J.; Lo, Y. S.; Ponzi, D. R.; Schwarzel, W. C. *J. Org. Chem.* **1977**, *42*, 4045.
(3) Dininno, F.; Beattie, T. R.; Christensen, B. G. *J. Org. Chem.* **1977**, *42*, 2960.
(4) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 553.
(5) Cignarella, G.; Pifferi, G.; Testa, E. *J. Org. Chem.* **1962**, *27*, 2668.
(6) Micetich, R. G.; Maiti, S. N.; Tanaka, M.; Yamazaki, T.; Ogawa, K. *J. Org. Chem.* **1987**, *51*, 853.
(7) Manhas, M. S.; Khajavi, M. S.; Bari, S. S.; Bose, A. K. *Tetrahedron Lett.* **1983**, *24*, 2323.

0022-3263/87/1952-3659$01.50/0 

**Scheme IV**




Similarly the 3,3-dibromoazetidinone[8] **12** was converted by method A to the trans product **13** (46%) exclusively and via method C to the cis product **14** (44%) as the major diastereomer (6:1).

In all of the above free radical reactions, the use of tributyltin hydride gave considerable amounts of reduction product **7** or **15**. In order to avoid this major side reaction, we investigated the use of allyltributyltin, which acts as both the olefinic substrate and tin radical chain propagator ($S_H2'$).[9]

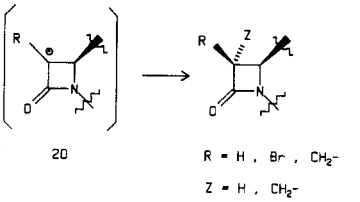
Reaction of either the *cis*- or *trans*-6-bromopenicillanate with allyltributyltin and azobisisobutyronitrile (AIBN) gave 95% of the 6$\alpha$-allylpenicillanate **16** as the only detectable diastereomer (Scheme IV). Reaction of 6,6-dibromopenicillanate **5** with allyltributyltin hydride and AIBN gave the 6$\beta$-bromo-6$\alpha$-allylpenicillanate **18** (60%) and 6,6-diallylpenicillanate **17** (22%). Reduction of this mixture using tributyltin hydride transformed **18** into the 6$\beta$-allylpenicillanate **19** as the only diastereomer in high yield. Also the above reactions did not proceed in the presence of a radical scavenger such as 2,6-di-*tert*-butyl-4-methylphenol (BHT), confirming a radical mechanism.

The reaction rate for the above process $S_H2'$ (see Experimental Section) was observed to be much faster than that obtained from simple alkyl halides and allyltributyltin (8 h at 80 °C).[10] The rate of conversion of **5** to **18** was about three times faster[11] than that of **4** to **16**. Since a bromine substituent will destabilize the radical intermediate **20** more than an alkyl or hydrogen substituent, we can therefore postulate that the rate of reaction increases with an increase in radical stabilization for the above $S_H2'$ process.

The mechanism of the reaction must involve a radical intermediate such as **20** which either adds onto an olefinic bond or abstracts the hydrogen from tributyltin hydride, from the less hindered side of the azetidinone moiety (Scheme V). The minor diastereomer **9** (or **14**) formed from method C most likely results from some reduction of **5** to **6**, which then adds onto olefin **8**.

In summary, the tributyltin-mediated addition of a 3-azetidinyl or 6-penicillanyl radical to allyltributyltin or

**Scheme V**




electrophilic olefins **8** constitutes a mild and stereoselective method for introducing alkyl side chains to azetidinones.

## Experimental Section

The NMR spectra were recorded on a Varian XL-200 or XL-300 spectrometer using $Me_4Si$ as internal standard and chloroform as the solvent. The chemical shift ($\delta$) and coupling constant ($J$) are quoted in ppm and hertz, respectively, and their assignments were determined unambiguously by decoupling, NOE, or 2D experiments when necessary. The infrared spectra (IR) were recorded on Perkin-Elmer 297 and the values ($\nu_{max}$) quoted in $cm^{-1}$. Mass spectra (MS) were obtained on MP 5984A or LKB 9000 spectrometers, ion source 250 °C and 70 eV electron impact, direct inlet: $m/z$ (assignment, relative intensity). Melting points were determined on a Gallenkamp block and are uncorrected. Column chromatography was performed with Woelm Silica 32–63 $\mu$m size.

**Benzhydryl 6,6-Dibromopenicillanate (5).** Diphenyldiazomethane (1.5 g, 7.7 mmol) and ethyl acetate (50 mL) were added dropwise to a mixture of 6,6-dibromopenicillanic acid (2.7 g, 7.6 mmol) and ethyl acetate (50 mL) at room temperature. The mixture was stirred overnight, and the excess diphenyldiazomethane was destroyed with a dropwise addition of acetic acid until the red solution decolorized to faint yellow. The product was then purified by flash chromatography to give 3.4 g (87%) of product as colorless crystals: mp 155–157 °C; IR (KBr) 1795 ($CO_2$), 1754 (azetidinone); $^1H$ NMR 1.31 and 1.56 (s, 3 H, $CH_3$), 4.87 (s, $C_3$-H), 6.09 (s, 1 H, $C_5$-H), 7.28 (s, 1 H, $CO_2CH$), 7.4–7.66 (m, 10 H, Ar H); MS (175 °C), 523/525/527 ($M^+$, 0.5/1.0/0.5), 444/446 ($M^{\bullet+}$ – $Br^\bullet$, 0.4/0.4), 167 (100), 152 (209), 114 (18); high-resolution MS (205 °C), calcd for $C_{21}H_{19}NO_3SBr_2$ 524.9433, found 524.9424.

**Benzhydryl 6$\alpha$-Bromopenicillanate (4).** With the same procedure as above, 6$\alpha$-bromopenicillanic acid was converted to the benzhydryl ester in 83% yield as light yellow crystals: mp 94–96 °C; IR (KBr) 1787 and 1749; $^1H$ NMR 1.27 and 1.66 (s, 3 H, $CH_3$), 4.62 (s, 1 H, $C_3$-H), 5.33 (d, 1 H, $C_5$-H, $J$ = 4), 5.59 (d, 1 H, $C_6$-H, $J$ = 4), 6.94 (s, 1 H, COOCH), 7.33–7.37 (br s, 10 H, Ar H); MS (130 °C), 445/447 ($M^+$, 1.7), 366 ($M^{\bullet+}$ – $Br^\bullet$, 0.3), 234/236 (6.0), 167 (100); high-resolution MS (130 °C), calcd for $C_{21}H_{20}NO_3SBr$ 447.0328, found 447.0355.

**Benzhydryl 6$\beta$-Bromopenicillanate (6).** 6,6-Dibromopenicillanate **5** (100 mg, 0.22 mmol), benzene (10 mL), and tributyltin hydride (91 mg, 0.31 mmol) were heated to 65 °C under a nitrogen atmosphere for 5 h. The solvent was removed and the residue dissolved in 30 mL of acetonitrile and washed three times with hexanes (30 mL). The solvent was then removed and the residue purified by column chromatography using ethyl acetate–hexanes (1:5) as eluant to give 19 mg of 6,6-dihydropenicillanate **7** (27%) and 70 mg of 6$\beta$-bromopenicillanate **6** (73%) as oils.

**6$\beta$-Bromopenicillanate 6**: IR ($CCl_4$) 1792 and 1751; $^1H$ NMR 1.30 and 1.60 (s, 3 H, $CH_3$), 4.66 (s, 1 H, $C_3$-H), 4.78 (s, 1 H, COOCH), 7.26–7.46 (br s, 10 H, Ar H); MS (108 °C), 445/447 ($M^+$, 0.1), 307/309 (5.6) 197 (10), 188 (76.3), 184 (67.1), 167 (45.5), 105 (100).

**6,6-Dihydropenicillanate 7**: $^1H$ NMR 1.23 and 1.49 (s, 3 H, $CH_3$), 3.03 (dd, 1 H, $C_6$-H, $J$ = 2, 16), 3.62 (dd, 1 H, $C_6$-H, $J$ = 4, 16), 4.54 (s, 1 H, $C_3$-H), 5.27 (dd, 1 H, $C_5$-H, $J$ = 2, 4), 6.91 (s, 1 H, COOCH), 7.31–7.34 (br s, 10 H, Ar H).

**General Procedure for the Reaction of 4 or 6 with Olefin 8. Method A.** Benzhydryl 6$\alpha$-bromopenicillanate (**4**; 200 mg, 0.45 mmol), dry benzene (5 mL), and methyl acrylate (0.58 g, 6.7 mmol) were refluxed under a nitrogen atmosphere. To this mixture were added tributyltin hydride (157 mg, 0.54 mmol), benzene (2 mL), AIBN (2 mg), and methyl acrylate (380 mg, 4.5

(8) The dibromo monolactam **12** was prepared in low yields by using the procedure given in ref 7.

(9) (a) Keck, G. E.; Enholm, E. J.; Yates, J. B.; Wiley, M. R. *Tetrahedron* **1985**, *41*, 4079. (b) Hanessian, S.; Alpegiani, M. *Tetrahedron Lett.* **1986**, 4857.

(10) Keck, G. E.; Yates, J. B. *J. Am. Chem. Soc.* **1982**, *104*, 5829.

(11) The relative rates of reactions **4** to **16** and **5** to **18** were measured by $^1H$ NMR, by using equimolar amounts of the bromo precursors and allyltributyltin with 15% AIBN in toluene-$d_8$ at 80 °C. The full kinetic analysis of both reactions will be reported elsewhere.

mmol) over a 5–6-h period (syringe pump). After the addition, the mixture was refluxed for 2 h and then cooled to room temperature. The solvent and excess methyl acrylate was removed. The residue was dissolved in acetonitrile (50 mL) and washed three times with hexanes (50 mL). The solvent was then removed and the residue purified by chromatography using ethyl acetate–hexanes (1:4) as eluant to give 132 mg (65%) of 6α-(2-carbomethoxyethyl)penicillanate **9d**, mp 84–85 °C.

**Method B.** Benzhydryl 6,6-dibromopenicillanate (**5**; 200 mg, 0.38 mmol), benzene (4 mL) and tributyltin hydride (115 mg, 0.40 mmol) were heated at 65 °C under nitrogen for 5 h. To this mixture was then added acrylonitrile (424 mg, 7.6 mmol) followed by a dropwise addition of tributyltin hydride (155 mg, 0.53 mmol), benzene (1 mL), and AIBN (2 mg) over a 5–6-h period. The mixture was cooled to room temperature and the solvent removed. The residue was dissolved in acetonitrile (50 mL) and washed three times with hexanes (50 mL). The solvent was removed and the residue purified by chromatography using ethyl acetate–hexanes (1:4) as eluant, giving 91 mg (48%) of 6α-(2-cyanoethyl)-penicillanate **9a** as an oil. Crystallization with $CCl_4$ and hexane gave a colorless product: mp 132 °C.

**Method C.** Benzhydryl 6,6-dibromopenicillanate (**5**; 200 mg, 0.38 mmol), benzene (4 mL), and acrylonitrile (424 mg, 7.6 mmol) were heated under a nitrogen atmosphere. To this mixture were added dropwise tributyltin hydride (115 mg, 0.40 mmol), benzene (1 mL), and AIBN (2 mg) over a 5–6-h period. The mixture was cooled, and the solvent and excess acrylonitrile were removed. The residue was dissolved in dry benzene (10 mL), treated with tributyltin hydride (155 mg, 0.53 mmol) and AIBN (2 mg), and refluxed for 3 h under a nitrogen atmosphere. The mixture was cooled to room temperature, the solvent removed, and the residue purified by chromatography using ethyl acetate–hexanes (1:4) as eluant, giving 74 mg (47%) of 6β-(2-cyanoethyl)penicillanate **11c** as an oil.

**Benzhydryl 6α-(2′-cyanoethyl)penicillanate (9a)**: IR ($CCl_4$) 2249 (CN), 1740–1785 (br, CO); $^1H$ NMR 1.26 and 1.62 (s, 3 H, $CH_3$), 2.22 (m, 2 H, $C_{1'}$-H), 2.54 (dt, 2 H, $C_{2'}$-H, $J$ = 3, 7), 3.40 (dt, 1 H, $C_6$-H, $J$ = 2, 7), 4.58 (s, 1 H, $C_3$-H), 5.13 (d, 1 H, $C_5$-H, $J$ = 2), 6.94 (s, 1 H, OCH), 7.35 (br s, 10 H, Ar H); MS (190 °C), 420 ($M^+$, 8.0), 380 (6), 209 (9.2), 168 (41.9), 167 (100); high-resolution MS (190 °C), calcd for $C_{24}H_{24}O_3N_2S$ 420.1507, found 420.1547.

**Benzhydryl 6β-(2′-cyanoethyl)penicillanate (11c)**: IR ($CCl_4$) 2248, 1742–1775; $^1H$ NMR 1.26 and 1.60 (s, 3 H, $CH_3$), 2.17 (m, 2 H, $C_{1'}$-H), 2.50 (t, 2 H, $C_{2'}$-H), 3.69 (dt, 1 H, $C_6$-H, $J$ = 4, 8), 4.50 (s, 1 H, $C_3$-H), 5.51 (d, 1 H, $C_5$-H, $J$ = 4), 6.94 (s, 1 H, COOCH), 7.31–7.36 (m, 10 H, Ar H).

**Benzhydryl 6α-(2′-carbomethoxyethyl)penicillanate (9d)**: IR ($CCl_4$) 1736–1770; $^1H$ NMR 1.24 and 1.61 (s, 3 H, $CH_3$), 2.16 (m, 2 H, $C_{2'}$-H), 2.50 (m, 2 H, $C_{1'}$-H), 3.35 (dt, 1 H, $C_6$-H, $J$ = 2, 8), 3.68 (s, 3 H, $COOCH_3$), 4.55 (s, 1 H, $C_3$-H), 5.07 (d, 1 H, $C_5$-H, $J$ = 2), 6.93 (s, 1 H, COOCH), 7.26–7.36 (m, 10 H, Ar H); MS (85 °C), 453 ($M^+$, 0.2), 371 (3.4), 279 (7.3), 227 (27.6), 194 (65.9), 167 (88.4); high-resolution MS (100 °C), calcd for $C_{25}H_{27}O_5NS$ 453.1609, found 453.1610.

**Benzhydryl 6β-(2′-carbomethoxyethyl)penicillanate (11e)**: IR ($CCl_4$) 1734–1771; $^1H$ NMR 1.29 and 1.66 (s, 3 H, $CH_3$), 2.10 (m, 2 H, $C_{1'}$-H), 2.37 (s, 2 H, $C_{2'}$-H), 3.65 (m, 1 H, $C_6$-H), 3.71 (s, 3 H, $OCH_3$), 4.50 (s, 1 H, $C_3$-H), 5.47 (d, 1 H, $C_5$-H, $J$ = 4), 6.95 (s, 1 H, OCH), 7.30–7.40 (m, 10 H, Ar H).

**Benzhydryl 6α-(2′-acetoxyethyl)penicillanate (9f)**: IR ($CCl_4$) 1740, 1772; $^1H$ NMR 1.24 and 1.61 (s, 3 H, $CH_3$), 2.03 (s, 3 H, $COCH_3$), 2.19 (m, 2 H, $C_{1'}$-H), 3.36 (dt, 1 H, $C_6$-H, $J$ = 2, 6), 4.18 (m, 2 H, $C_{2'}$-H), 4.56 (s, 1 H, $C_3$-H), 5.13 (d, 1 H, $C_7$-H, $J$ = 2), 6.92 (s, 1 H, OCH), 7.26–7.36 (m, 10 H, Ar H); MS (110 °C), 453 ($M^+$, 1.6), 425 (0.9), 244 (5.1), 188 (34), 168 (39), 167 (100).

**Benzhydryl 6β-(2′-acetoxyethyl)penicillanate (11g)**: IR ($CCl_4$) 1741, 1772; $^1H$ NMR 1.24 and 1.63 (s, 3 H, $CH_3$), 2.04 (s, 3 H, $COCH_3$), 2.18 (m, 2 H, $C_{1'}$-H), 3.67 (m, 1 H, $C_5$-H), 4.13 (m, 2 H, $C_{2'}$-H), 4.49 (s, 1 H, $C_3$-H), 5.46 (d, 1 H, $C_6$-H, $J$ = 4.5), 6.93 (s, 1 H, OCH), 7.24–7.37 (m, 10 H, Ar H).

***N*-(*p*-Methoxyphenyl)-3,3-dibromo-4-styrylazetidinone (12)**: IR ($CCl_4$) 1782 (azetidinone); $^1H$ NMR 3.76 (s, 3 H, $OCH_3$), 5.08 (d, 1 H, $C_4$-H, $J$ = 8), 6.18 (dd, 1 H, $C_5$-H, $J$ = 8, 16), 6.85 (s, 1 H, $C_6$-H, $J$ = 16), 6.97–7.49 (m, 9 H, Ar H); MS (175 °C), 435/437/439 ($M^+$, 1.2/2.6/1.3), 356/358 ($M^{\bullet+}$ – $Br^{\bullet}$, 3.6/3.7), 249 (16.9), 237 (15), 149 (52), 128 (100).

***N*-(*p*-Methoxyphenyl)-3α-(2′-carbomethoxyethyl)-4-styrylazetidinone (13)**: IR 1742 (CO); $^1H$ NMR 2.21 (t, 2 H, $C_{1'}$-H), 2.56 (m, 2 H, $C_{2'}$-H), 3.13 (dt, 1 H, $C_3$-H, $J$ = 2, 8), 3.69 (s, 3 H, $COOCH_3$), 3.77 (s, 3 H, $OCH_3$), 4.33 (dd, 1 H, $C_4$-H, $J$ = 2, 8), 6.29 (dd, 1 H, $C_5$-H, $J$ = 8, 16), 6.76 (d, 1 H, C6-H), 7.24–7.45 (m, 9 H, Ar H); MS (85 °C), 365 ($M^+$, 1.2), 313 (14), 281 (18), 280 (22), 149 (73), 130 (100); high-resolution MS (85 °C), calcd for $C_{22}H_{23}O_4N$ 365.1627, found 365.1644.

***N*-(*p*-Methoxyphenyl)-4-styrylazetidinone (15)**: IR ($CCl_4$) 1740 (CO); $^1H$ NMR 2.93 (dd, 1 H, $C_3$-H, $J$ = 2, 16), 3.41 (dd, 1 H, $C_3$-H, $J$ = 4, 16), 3.77 (s, 3 H, $OCH_3$), 4.64 (m, 1 H, $C_4$-H), 6.31 (dd, 1 H, $C_5$-H, $J$ = 8, 16), 6.83 (d, 1 H, $C_6$-H, $J$ = 16), 7.23–7.45 (m, 9 H, Ar H); MS (85 °C), 279 ($M^+$, 1.0), 237 (7.0), 172 (2.6), 149 (50.8), 130 (100).

**Benzhydryl 6α-Allylpenicillanate (16).** Benzhydryl 6-bromopenicillinate **4** or **6** (50 mg, 0.11 mmol), toluene (0.4 mL), allyltributyltin (74 mg, 0.22 mmol), and AIBN (2.4 mg) were warmed to 65 °C under a nitrogen atmosphere for 45 min. The solvent was removed and the residue worked up as before, giving 43 mg (95%) of product as an oil: IR (neat) 1750, 1772; $^1H$ NMR 1.24 and 1.62 (s, 3 H, $CH_3$), 2.58 (m, 2 H, $C_{1'}$-H), 3.38 (dt, 1 H, $C_6$-H, $J$ = 2, 7), 4.57 (s, 1 H, C3-H), 5.09–5.17 (m, 3 H, $C_6$-H and $C_{3'}$-H), 5.79 (m, 1 H, $C_{2'}$-H), 6.93 (s, 1 H, COOCH), 7.26–7.4 (m, 10 H, Ar H); MS (95 °C), 407 ($M^+$, 11), 379 (1.0), 326 (1.9), 240 (3.0), 168 (48.2), 167 (100); high-resolution MS (105 °C), calcd for $C_{24}H_{25}O_3NS$ 407.1555, found 407.1562.

**Benzhydryl 6β-Allyl- (19) and 6,6-Diallylpenicillanate (17).** Benzhydryl 6,6-dibromopenicillanate (**5**) (53 mg, 0.10 mmol), toluene (0.4 mL), allyltributyltin (64 mg, 0.20 mmol), and AIBN (2.4 mg) were warmed to 65 °C under a nitrogen atmosphere for 15 min. The solvent was removed and the residue dissolved in acetonitrile (15 mL) and washed with hexanes (20 mL). The solvent was removed to give a mixture of 6α-allyl-6β-bromopenicillanate (**18**) and 6,6-diallylpenicillanate **17**, which could not be separated by column chromatography. To the above mixture were then added tributyltin hydride (44 mg, 0.15 mmol), benzene (10 mL), and AIBN (catalytic) and refluxed for 2 h. The mixture was cooled to room temperature and the solvent removed. After the usual workup and column chromatography, 30 mg of 6β-allylpenicillanate **19** and 9 mg of 6,6-diallylpenicillanate **17** were obtained as oils.

**Benzylhydryl 6β-allylpenicillanate (19)**: IR (neat) 1749, 1773; $^1H$ NMR 1.25 and 1.62 (s, 3 H, $CH_3$), 2.53 (t, 2 H, $C_{1'}$-H, $J$ = 8), 3.68 (dt, 1 H, $C_6$-H, $J$ = 4, 8), 4.48 (s, 1 H, $C_3$-H), 5.05–5.12 (m, 2 H, $C_{3'}$-H), 5.44 (d, 1 H, $C_5$-H, $J$ = 4), 5.75 (m, 1 H, $C_{2'}$-H), 6.94 (s, 1 H, COOCH), 7.26–7.34 (m, 10 H, Ar H); MS (115 °C) (chemical ionization, ammonia), 425 (M + $NH_4^+$, 0.4), 392 (0.2), 391 (0.8), 168 (14), 167 (100).

**Benzhydryl 6,6-diallylpenicillanate (17)**: IR (neat) 1730–1780 (br); $^1H$ NMR 1.24 and 1.61 (s, 3 H, $CH_3$), 2.53 (m, 4 H, $C_{1'}$-H), 4.48 (s, 1 H, $C_3$-H), 5.11–5.19 (m, 5 H, $C_5$-H and $C_{3'}$-H), 5.81 (m, 2 H, $C_{2'}$-H), 6.92 (s, 1 H, COOCH), 7.25–7.35 (m, 10 H, Ar H); MS (95 °C), 447 ($M^+$, 0.2), 408 (0.7), 407 (2.4), 326 (3.0), 240 (1.9), 168 (35.6), 167 (100); high-resolution MS (100 °C), calcd for $C_{27}H_{29}O_3NS$ 447.1867, found 447.1833.

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