975 cm^{-1}; NMR (Me_2SO-d_6/D_2O) δ 7.78–6.93 (aromatic protons, 6), 5.7 and 5.41 (H-9 and H-10, 2, indicative of a trans–cis mixture in a ratio of 30:70), 3.85 (s, 6, OCH_3).

1,4-Diethoxy-9,10-dihydro-9,10-anthracenediol (12): 90% yield: mp 112–114 °C; IR 3520 (s), 1000 cm^{-1}; NMR (Me_2SO-d_6/D_2O) δ 7.86–7.38 (aromatic protons, 4), 7.08 (s, 2, H-2 and H-3), 6.0 and 5.91 (s, 2, H-9 and H-10), 4.2 (q, 4, methylene protons), 1.41 (t, 6, methyl).

1,5-Diethoxy-9,10-dihydro-9,10-anthracenediol (14): 90% yield; mp 211–215 °C; IR 3520 (s), 3360 (br), 1580, 1010, 980 cm^{-1}; NMR (Me_2SO-d_6/D_2O) δ 7.58–6.98 (aromatic protons, 6), 5.98 and 5.90 (H-9 and H-10, 2, in a 1:3 ratio), 4.5–3.83 (2 overlapping q, 4, methylene protons), 1.6–1.21 (2 overlapping t, 6, methyl protons).

1,8-Diethoxy-9,10-dihydro-9,10-anthracenediol (16): 90% yield; mp 228–230 °C; IR OH centered at 3390 cm^{-1}, 1590, 1040, 980 cm^{-1}; NMR (Me_2SO-d_6/D_2O) δ 7.55–6.91 (aromatic protons, 6), 6.61, 6.40, 5.88, 5.50 (H-9 and H-10, 2, in a ratio of 8:3:8:3), 4.46–3.93 (2 overlapping q, 4, methylene protons), 1.38 (t, 6, methyl protons).

4,5-Dichloro-9-anthrone (18): 75% yield; mp 188–190 °C (lit.[19] mp 198 °C); NMR ($CDCl_3$) δ 8.30 (dd, 2, H-1 and H-8), 7.83–7.3 (m, 4, remaining aromatic protons), 4.21 (s, 2, methylene protons). These values are in agreement with published NMR data.[9]

1,5-Dichloro-9,10-dihydro-9,10-anthracenediol (20) was obtained in 90% yield: mp 215–216 °C (lit.[7] mp 215–220 °C); IR OH centered at 3200, 980 cm^{-1}; NMR (Me_2SO-d_6/D_2O) δ 7.83–7.5 (aromatic protons, 6), 5.90 (s, 2, H-9 and H-10).

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Registry No. 1, 6119-74-0; 2, 50259-94-4; 2 acetate, 76403-00-4; 3, 6448-90-4; 4, 76403-01-5; 4 acetate, 76403-02-6; 5, 6407-55-2; 6, 76403-03-7; 7, 76403-04-8; 9, 963-96-2; *cis*-10, 76403-05-9; *trans*-10, 76403-06-0; 11, 75829-97-9; *trans*-12, 76403-07-1; 13, 22924-22-7; *cis*-14, 76403-08-2; *trans*-14, 76403-09-3; 15, 16294-26-1; *cis*-16, 76403-10-6; *trans*-16, 76403-11-7; 17, 82-43-9; 18, 63605-29-8; 19, 82-46-2; 20, 41187-73-9; 1,8-dimethoxyanthracene, 16294-34-1.

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Synthesis of 2-Azetidinones from Serinehydroxamates: Approaches to the Synthesis of 3-Aminonocardicinic Acid

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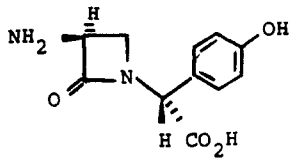
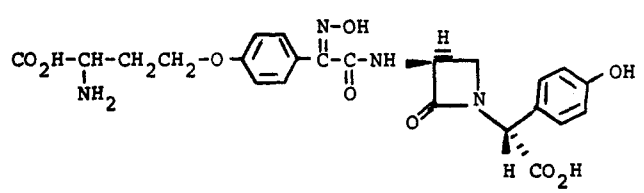
Protected forms of 3-aminonocardicinic acid (3-ANA, 1) have been synthesized in a short and efficient manner from L-serine. The serine derived *O*-benzyl hydroxamate **4** was cyclized to the 1-(benzyloxy)-2-azetidinone **5** with $Ph_3P/CCl_4/Et_3N$. N–O reduction gave the N-unsubstituted 2-azetidinone **6**. While conventional methods proved unsatisfactory for the N-alkylations of **6**, both phase-transfer-catalyzed alkylation and rhodium acetate catalyzed carbenoid insertion provided 3-ANA derivatives in good yield. Other alkylation methods and studies related to deprotection of the 3-ANA derivatives are also described.

3-Aminonocardicinic acid (3-ANA, 1) has been utilized as the key intermediate in the synthesis of nocardicin A (**2**),[1] a member of the nocardicin family of unusual monocyclic β-lactam antibiotics. Previous approaches to the synthesis of 3-ANA have used now-classical methods for the formation of the 2-azetidinone nucleus, including ketene–imine cycloaddition[2] and cyclization of β-halo amides.[3] Our approach to 3-ANA (Scheme I) relies on the efficient preparation of the N-unsubstituted β-lactam **6** from readily available, chiral starting materials, followed by subsequent alkylation of the β-lactam nitrogen.



1, 3-ANA



2

We chose as our starting material *N*-(*tert*-butoxycarbonyl)-L-serine (**3**). As previously reported,[4] compound **3** was directly coupled with *O*-benzylhydroxylamine in the presence of a carbodiimide. The product, **4**, was cyclized to **5** with $Ph_3P/CCl_4/Et_3N$. Sequential reduction of **5** with H_2–Pd/C and $TiCl_3$[5] gave 3-[(*tert*-butoxycarbonyl)-amino]-2-azetidinone (**6**) in 67% overall yield from **3**.

A review of the literature revealed that alkylation of N-unsubstituted β-lactams on nitrogen is not consistently efficient.[6] Strong bases (NaH, $NaNH_2$, *n*-BuLi, and

(1) (a) Aoki, H.; Sakai, H.; Kohsaka, M.; Konomi, T.; Hosada, J.; Kubochi, Y.; Iguchi, E. *J. Antibiot.* **1976**, *29*, 492–500; (b) Hashimoto, M.; Komori, T.; Kamiya, T. *Ibid.* **1976**, *29*, 890–901.

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(3) (a) Koppel, G. A.; McShane, L.; Jose, F.; Cooper, R. D. G. *J. Am. Chem. Soc.* **1978**, *100*, 3933–3935; (b) Wasserman, H. H.; Hlasta, D. L. *Ibid.* **1978**, *100*, 6780; (c) Wasserman, H. H.; Hlasta, D. L.; Tremper, A. W.; Wu, J. S. *Tetrahedron Lett.* **1979**, 549–552.

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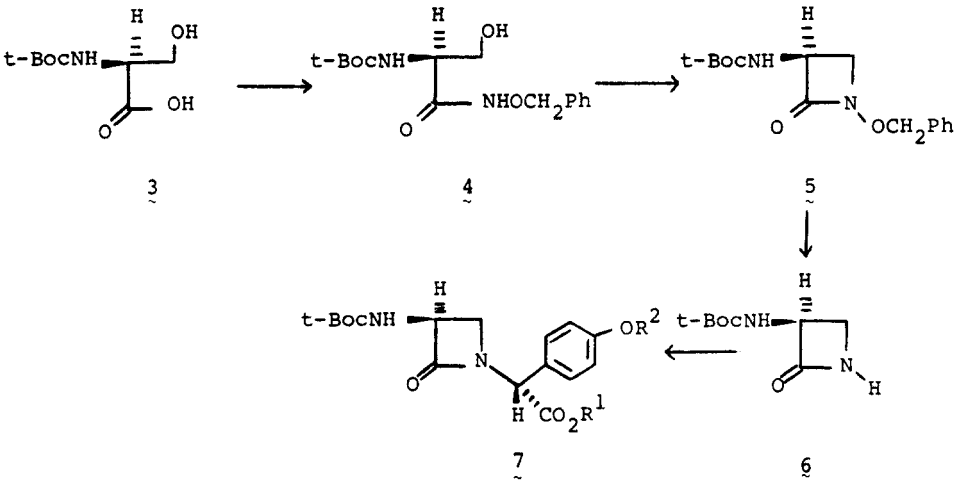
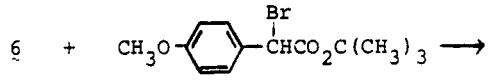
0022-3263/81/1946-1557$01.25/0

Scheme I

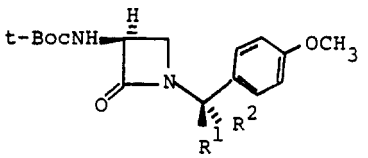


others) have been employed with simple systems, but such basic conditions tend to polymerize or racemize **6**. Kamiya has reported a very low yield (<11%) in the alkylation of 3-(phenylacetylamino)-2-azetidinone (obtained from penicillin degradation) with methyl α-bromo-(*p*-methoxyphenyl)acetate using NaH/DMF.[7] Three alternative methods for β-lactam N-alkylation were therefore explored: phase-transfer-catalyzed (PTC) alkylation, addition to a reactive quinone methide, and carbenoid insertion into the β-lactam amide N–H bond.

Phase-Transfer-Catalyzed Alkylation. Phase-transfer catalysis has been used by many workers to carry out both intra- and intermolecular alkylations of β-lactams.[8] As illustrated by the procedure of Reuschling et al.,[9] intermolecular alkylations of β-lactams were efficient when no heteroatom substituent was present at C_3. We employed the same methodology for the alkylation of β-lactam **6** (eq 1). Thus **6** was treated with *tert*-butyl α-



9



(1)

7a R^1=H, R^2=$CO_2C(CH_3)_3$

8a R^1=$CO_2C(CH_3)_3$, R^2=H

bromo-(*p*-methoxyphenyl)acetate (**9**) in the presence of powdered KOH and 10 mol % of benzyltriethylammonium chloride. After preparative TLC, a 35% yield of *tert*-butyl 3-[(*tert*-butoxycarbonyl)amino]-*p*-methoxy-3-aminonocardicinate was isolated as a 2:1 mixture of diastereomers (**7a**, **8a**). The major isomer **7a** was separated by crystallization from ethyl acetate–hexanes. Structural assignments were made by comparison of NMR data with reported compounds.[10] The optimum amount of catalyst for this reaction was found to be 2–10 mol %. Deviations from this range resulted in less efficient alkylation. The use of nonnucleophilic bases (K_2CO_3 or Et_3N) was not effective. However, slow, separate additions of solutions of tetra-*n*-butylammonium hydroxide and a mixture of β-lactam **6** and bromide **9** to excess **9** also gave a similar mixture of **7a** and **8a** in 42% isolated yield.

In all PTC alkylations carried out, two serious side reactions were seen that account for the moderate yield of **7a** and **8a**. Both the β-lactam and the alkyl halide undergo base-catalyzed reaction to give either dimeric or polymeric material (Scheme II). Nucleophilic opening of **6** by hydroxide ion is facilitated by the inductive effects of the carbamate at C-3. The formation of polyamides from β-lactams has much precedent.[11] Bromide **9** dimerized under the reaction conditions to give **11**. Upon silica gel chromatography, **11** was partially converted to alkene **12**. Presumably, dimerization resulted from abstraction of the acidic α-proton of **9** followed by nucleophilic substitution (path a) or elimination of Br^- to form the carbene **13** (path b).

While phase-transfer catalysis proved to be more efficient than use of strong base alone, the polymerization of the β-lactam with nucleophilic base was a serious drawback. Milder conditions were therefore sought.

Addition to a Quinone Methide. Nucleophiles react with quinone methide intermediates under both acid and base catalysis.[12] While N-unsubstituted β-lactams are very weak nucleophiles, they are known to condense with electron-deficient glyoxylic esters to form stable amidals[13] and to undergo intramolecular Michael addition with thioenols.[14] As seen in eq 2, quinone methide **14** could be viewed as a doubly vinylogous glyoxylic ester. Additionally, the bulky *t*-Boc group at C-3 in **6** was expected to influence the mode of addition to **14** to provide the less

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(10) See ref 2a and 3a,b.

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(13) (a) Scartazzini, R.; Peter, H.; Bickel, H.; Heusler, K.; Woodward, R. B. *Helv. Chim. Acta* **1972**, *55*, 408–417; (b) Scartazzini, R.; Gosteli, J.; Bickel, H.; Woodward, R. B. *Ibid.* **1972**, *55*, 2567–2572.

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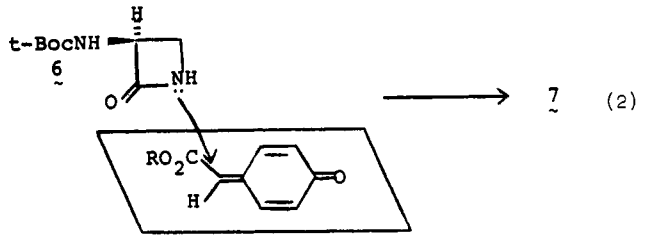
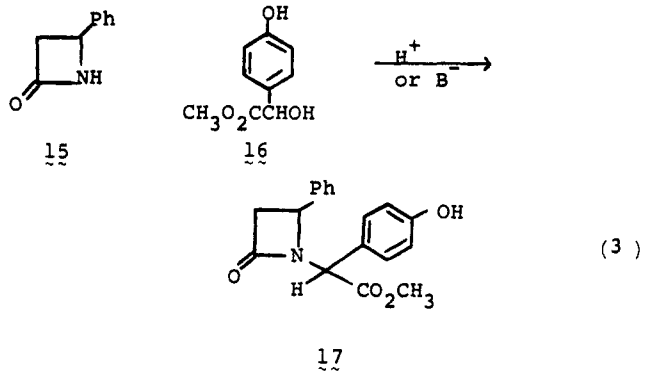


14

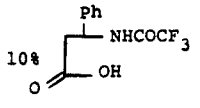
sterically hindered isomer of protected 3-ANA.

Among other methods, quinone methides have been generated by both acid and base catalysis.[12a,c] As a model reaction, 4-phenyl-2-azetidinone (**15**) was reacted with methyl *p*-hydroxymandelate (**16**) under a variety of acidic (TFA) and basic conditions (K_2CO_3, Et_3N, or KOH: eq 3). Under none of the conditions tested was the addition



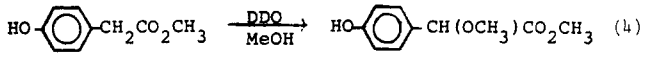
15 16 17 (3)

product **17** detected. Two interesting observations were noted, however. First, treatment of **15** with KOH and the phase-transfer catalyst benzyltriethylammonium chloride (BTAC) did not result in polymer formation,[15] as was seen with **6**, thus pointing again to the carbonyl activating effect of the carbamate in **6**. Second, when **15** was treated with 150 mol % of trifluoroacetic acid at reflux, a 10% yield of the ring-opened material **18** was formed, presumably by trifluoroacetate attack on the protonated β-lactam.



18

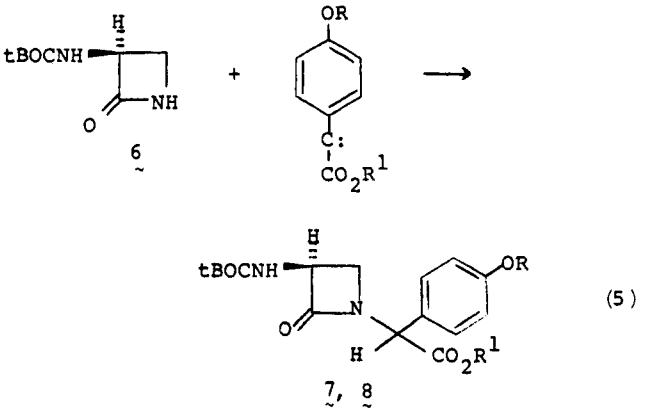
In no instance was evidence obtained for the formation of a quinone methide from **16**; therefore, another method of its generation was explored. 2,3-Dichloro-5,6-dicyanobenzoquinone (DDQ) has been used to convert *p*-hydroxybenzyl groups into quinone methides.[16] When methyl (*p*-hydroxyphenyl)acetate **19** was treated with DDQ in methanol (eq 4), a 37% yield of methyl α-meth-



19 20 (4)

oxy-(*p*-hydroxyphenyl)acetate (**20**) was isolated along with a mixture of starting material and products resulting from further oxidation of **20**. When **15** and **19** were treated with DDQ in CH_3CN, **15** was recovered quantitatively along with 10% of **19** and a complex mixture of H_2DDQ–**19** adducts. Thus, under the conditions employed, H_2DDQ appeared to be a better nucleophile than **15**.

Carbenoid Insertion. The conditions under which a carbenoid insertion into the N–H bond (eq 5) would take



6 7, 8 (5)

place were considered ideal for the acid- and base-sensitive β-lactam **6**. In addition, Ratcliffe et al.[17] have reported an efficient intramolecular insertion with a rhodium acetate catalyst.

As shown in Scheme III, the requisite α-diazo ester **22** was generated from the corresponding glyoxylate **21** by treatment with *p*-toluenesulfonylhydrazine, followed by base-induced elimination of *p*-toluenesulfinic acid (70–80% yield).[18a,b] Diazo transfer from *p*-toluenesulfonyl azide to *p*-alkoxymandelate esters under basic conditions was not effective; however, the recently reported phase-transfer-catalysis mediated diazo transfer[19] was not tried. When an excess of **22** was added to a mixture of **6** and a trace of $Rh_2(OAC)_4$ catalyst in refluxing benzene, a diastereomeric mixture resulted which was separated by crystallization or high-pressure LC. Treatment of the separated undesired isomer **8** with Et_3N provided a new equilibrium mixture of diastereomers **7** and **8** in a ratio of 4:3 from which more **7** was isolated. The acidity of the exocyclic methine proton of 3-ANA derivatives has been reported previously.[3] The overall yield of **7c** from *N*-(*tert*-butoxycarbonyl)-L-serine (**3**) was 45%.

Deprotection of 3-ANA Derivatives. In order to complete the synthesis of 3-ANA, we envisioned removing all the protecting groups in a single step. At least two reagents seemed applicable. Both iodotrimethylsilane and boron tribromide[21] have been reported to cleave carbamates, esters, and aryl ethers, but not amide bonds.

Both reagents efficiently cleaved the *tert*-butoxycarbonyl (*t*-Boc) group and *tert*-butyl esters of variously sustituted β-lactams [**7a,b** and **8a,b** → **23**, **24a,b** (R = H); eq 3]. However, the conditions necessary to remove the benzyl or ethyl ester or the methyl ether also brought about destruction of the β-lactam. Compound **7c** was therefore

(15) Compound **18** is readily alkylated under PTC conditions. See ref 9.

(16) (a) Becker, H. D. *J. Org. Chem.* **1965**, *30*, 982–989; (b) Buchan, G. M.; Findlay, J. W. A.; Turner, A. B. *J. Chem. Soc., Chem. Commun.* **1975**, 126–127; (c) Buchan, G. M.; Turner, A. B. *J. Chem. Soc., Perkin Trans. 1* **1979**, *5*, 1326–1332; (d) Becker, H. D.; Björk, A.; Adler, E. *J. Org. Chem.* **1980**, *45*, 1596–1600.

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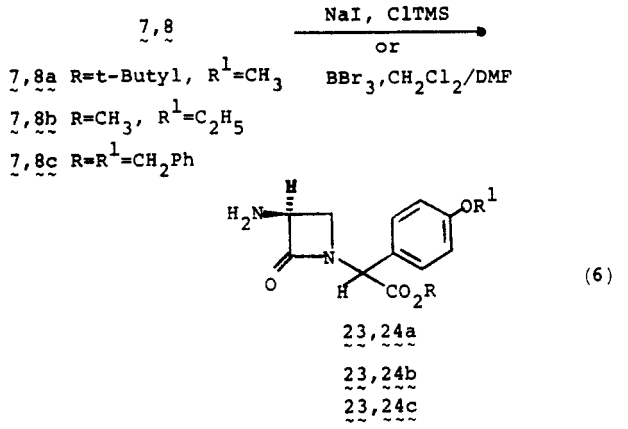
(22) See ref 3a.



(6)

treated with *p*-toluenesulfonic acid in ethyl acetate followed by neutralization with $NaHCO_3$ to give **23c** in 63% overall yield (Scheme IV). This material was identical by NMR with the dibenzyl derivative of 3-ANA previously reported[3a] and converted to 3-ANA with H_2–Pd/C.

An obvious modification which might allow a single-step deprotection via catalytic hydrogenation would be the replacement of the *t*-BocNH protecting group in **7c** with a carbobenzyloxy (CBz) group. In order to synthesize 3-[(carbobenzyloxy)amino]-2-azetidinone (**38**), we required a hydroxamate oxygen protecting group that could be removed in the presence of the CBz group. Ideally, the protecting group would be removable under the conditions of the $TiCl_3$ reduction (pH 4–10). Three O-protected hydroxamates were tested (Scheme V). As a model reaction, **31** was prepared in 57% yield from 2,2-dimethyl-3-hydroxypropanoic acid (**25**) and *O*-pivaloylhydroxylamine (OPHA). OPHA was chosen because simple, unhindered *O*-acylhydroxylamines are known to be unstable.[23] The conversion of **31** to **36** was readily accomplished by the in situ aminolysis of the pivaloyl group and subsequent N–O bond reduction in a mixture of $(NH_4)_2CO_3$–Na_2CO_3–$TiCl_3$ at pH 7.5. When the 3-CBzNH derivative **32**, obtained from *N*-(carbobenzyloxy)-L-serine (**26**) and OPHA in 61% yield, was treated similarly, a mixture was obtained in which no **37** or **38** was present. In this case, aminolysis of the β-lactam and carbamate appeared to be faster than that of the pivaloyl group. Acid- and base-catalyzed treatment of **28** also failed to yield the *N*-hydroxy β-lactam **37**.

The *O*-*tert*-butyl and *O*-trityl β-lactams **33** and **34** were prepared in 63% and 56% yields, respectively, from *N*-(carbobenzyloxy)-L-serine (**26**) and the corresponding hydroxylamine. While the yields were somewhat lower with these sterically hindered hydroxylamines, no O-alkylated products were detected in the cyclization reaction.[24] Both *O*-*tert*-butyl[25] and *O*-trityl[26] hydroxamates have been deprotected by mild acid; however, **33** did not react with 100 mol % of trifluoroacetic acid (TFA) in CH_2Cl_2 over 8 days at room temperature. When **33** was dissolved in neat TFA with 100 mol % of anisole, a mixture resulted that contained no β-lactam. Compound **34** yielded 64% trityl chloride when treated with HCl gas in benzene. A hygroscopic precipitate also formed which has not been rigorously characterized. Thus, straightforward preliminary attempts to prepare a more versatile intermediate such as **38** were not successful.

Conclusion

We have developed a short and efficient (28% overall yield for **3** → **23**) method for the synthesis of 3-ANA from readily available chiral starting materials (Scheme I). The novel properties of O-substituted serine hydroxamates facilitated the efficient, biomimetic bond closure of the β-lactam. The sequential reduction of the N–O bond of **5** led to 3-(*t*-Boc-amino)-2-azetidinone (**6**) which was labile to both acid- and base-catalyzed ring opening. While the use of PTC alkylation showed greatly improved yields over simple alkylations, the 3-ANA derivatives **7a–c** were more efficiently prepared by Rh_2OAc_4-catalyzed carbenoid insertion.

Experimental Section

General Comments. Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Infracord or 727b spectrometer. NMR spectra were determined in chloroform-*d* with tetramethylsilane as a reference unless otherwise stated on a Varian H-60A or XL-100 spectrometer. Mass spectra were recorded on a Du Pont DP102 spectrometer. Elemental analyses were performed by Midwest Microlabs or M-H-W Laboratories. High-pressure LC was performed by using a Beckman/Altex Model 332 chromatograph. Solvents used were dried and purified by standard methods.

***O*-Benzyl *N*-α-(*tert*-butoxycarbonyl)serinehydroxamate (4), 1-(benzyloxy)-3-[(*tert*-butoxycarbonyl)amino]-2-azetidinone (5), and 3-[(*tert*-butoxycarbonyl)amino]-2-azetidinone (4)** were prepared as reported earlier.[4,5]

***tert*-Butyl α-bromo-(*p*-methoxyphenyl)acetate (9)** was prepared by the method of Gotthardt et al.[27] Thus, 25 g (0.15 mol) of *p*-methoxyphenylacetic acid (Aldrich) was refluxed with 65 mL (1.2 mol) of thionyl chloride for 4 h. Distillation of the reaction mixture afforded 23 g (0.125 mol, 84%) of the acid chloride: bp 89 °C (200 μmHg) [lit.[27] bp 116–118.5 (5 mmHg)]; NMR δ 3.8 (3 H, s), 4.08 (2 H, s), 6.8–7.3 (5 H, q).

The acid chloride, dissolved in 250 mL of anhydrous ether, was added dropwise to a cooled solution of 25 g (0.24 mol) of Na_2CO_3 and 71 mL (0.75 mol) of *tert*-butyl alcohol in 250 mL of ether. After the mixture was stirred 4 h, the precipitated salts were filtered, and the ether was removed by rotoevaporator. The unreacted acid crystallized from ethyl acetate–hexanes selectively. Traces of acid were removed from the ester by a saturated $NaHCO_3$ wash. The ester (12.3 g, 0.05 mol; 34% from the acid) was thus isolated: NMR δ 1.3 (9 H, s), 3.46 (2 H, s), 3.75 (3 H, s), 6.8–7.3 (5 H, q).

Conversion to the bromide **9** was accomplished by refluxing 2 g (0.008 mol) of the ester with 1.5 g (0.008 mol) of *N*-bromosuccinimide in 25 mL of CCl_4 for 3 h. After the solvent was removed under reduced pressure, an oil remained that solidified in the freezer at −20 °C. Recrystallization from ethyl acetate–hexanes yielded 1.4 g (0.005 mol, 56%) of **9**: mp 61.5–63.0 °C; NMR δ 1.48 (9 H, s), 3.82 (3 H, s), 5.28 (1 H, s), 6.83–7.6 (5 H, m).

Phase-Transfer-Catalyzed Alkylation. Method A. Compound **6** (0.0893 g, 0.48 mmol) dissolved in 10 mL of acetonitrile with 0.1474 g (0.49 mmol) of **9** was added to a suspension of 0.367 g (0.55 mmol) of powdered KOH and 0.0118 g (0.05 mmol) of benzyltriethylammonium chloride in 15 mL of acetonitrile at 0 °C. The reaction was allowed to warm to room temperature and stirred for 24 h under a dry nitrogen atmosphere. The precipitated polyamide **10** was filtered: decomposes at 245 °C; IR (KBr) 3280, 1640 cm^{-1}; NMR (Me_2SO-d_6) δ 1.37 (9 H, s), 3.0–3.6 (2 H, br), 3.65–4.1 (1 H, br), 6.5–7.0 (1 H, br). Preparative TLC (silica, 20% ethyl acetate–80% hexanes) yielded 47 mg of a mixture of **11** [NMR ($DCCl_3$) δ 1.28 (18 H, s), 3.78 (6 H, s), 5.28 (1 H, s), 6.82–7.85

(23) (a) Miller, J. J.; DeBons, F. E.; Loudon, G. M. *J. Org. Chem.* **1977**, *42*, 1750–1761; (b) Miller, M. J.; Loudon, G. M. *J. Am. Chem. Soc.* **1975**, *97*, 5295–5297.

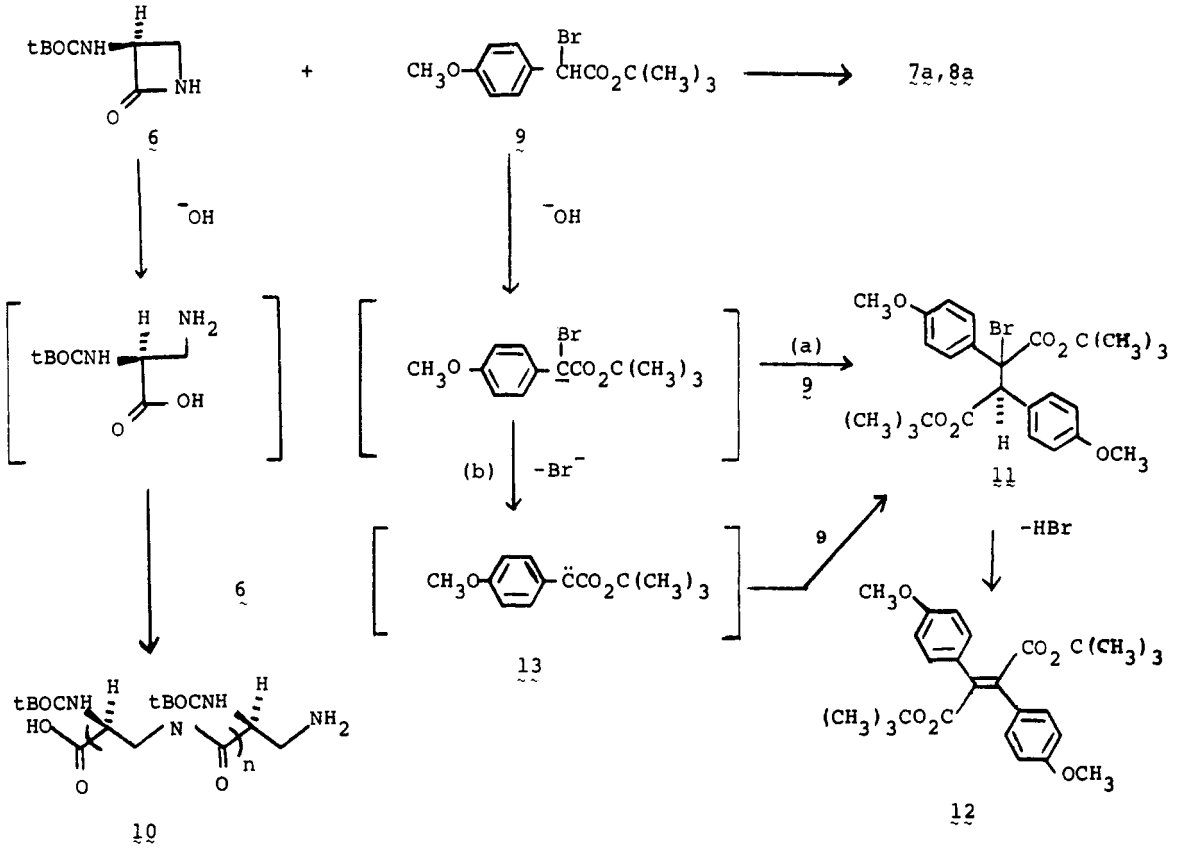
(24) The β-lactams **33** and **34** were reductively hydrolyzed to give L-2,3-diaminopropionic acid.[4] No L-serine from O-alkylated hydroxamate was detected by amino acid analysis.

(25) Kolasa, T.; Chimiak, A. T. *Tetrahedron* **1974**, *30*, 3591.

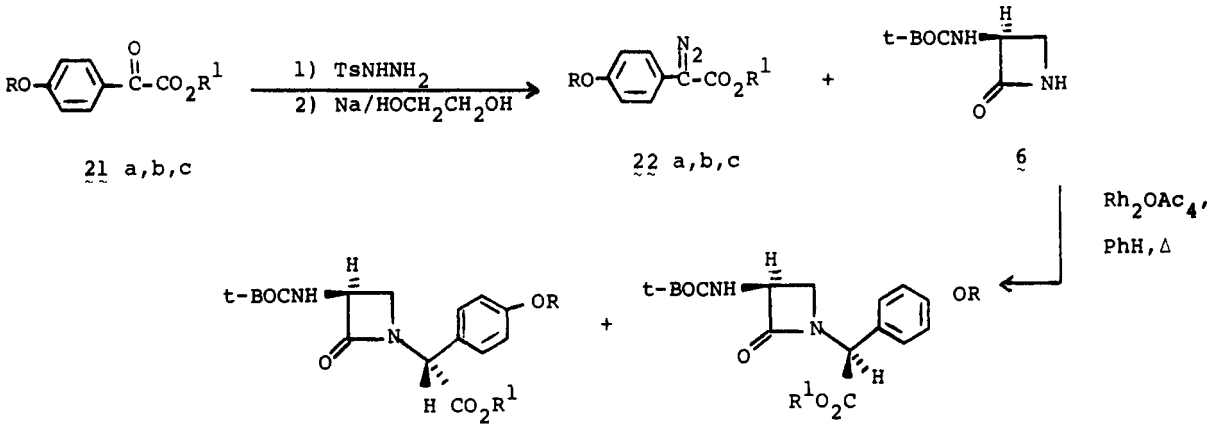
(26) Lutz, W. B. *J. Org. Chem.* **1971**, *36*, 3835–3837.

(27) Gotthardt, H.; Weisshuhn, M. L.; Christl, B. *Chem. Ber.* **1976**, *109*, 740–752.

Scheme II

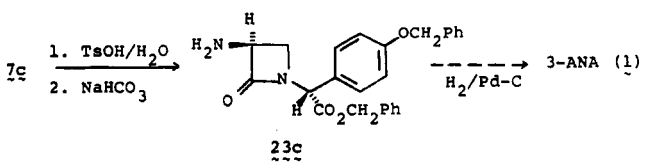


Scheme III



(a)	R = CH_3, R^1 = $-C(CH_3)_3$	26%	4:3
(b)	R = CH_3, R^1 = $-CH_2CH_3$	60%	4:3
(c)	R = R^1 = CH_2Ph	67%	1:1.2

Scheme IV

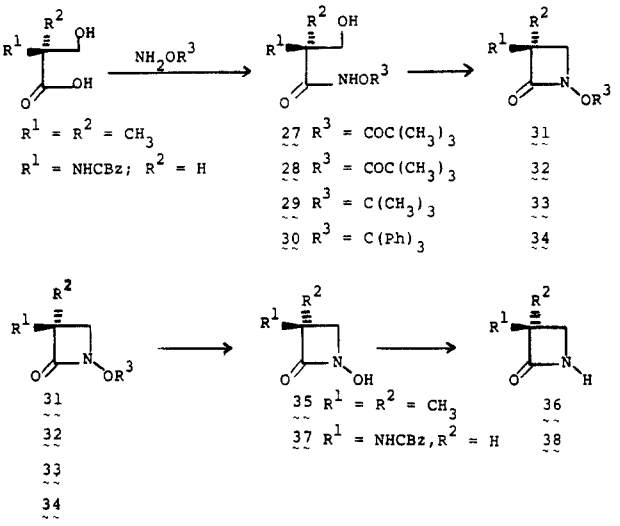


(8 H, m, para-disubstituted phenyl)] and **12** and 69.3 mg (0.17 mmol) of **7a** and **8a** (ratio 2:1). For **7a**: NMR (XL-100) δ 1.39 (9 H, s), 1.48 (9 H, s), 2.92–3.03 (1 H, dd, J = 2 Hz, β-H), 3.83 (3 H, s), 3.8–3.93 (1 H, t, J = 5 Hz, α-H), 4.92 (2 H, br, NH and NCH), 5.44 (2 H, s), 6.86–7.05 (5 H, m); IR (CCl_4) ν_{CO} 1760 cm^{-1}; mass spectrum (CI with argon), m/e 407 (M + 1); mp 132–133 °C (ethyl acetate–hexanes); $[\alpha]^{20}_D$ −110.5 ± 5° (c 0.51, CH_3OH). Anal. Calcd for $C_{21}H_{29}N_2O_6$: C, 62.07; H, 7.39; N, 6.90. Found: C, 62.07; H, 7.24; N, 7.01. For **8a** (oil): NMR (A60-A) δ 1.43 (18 H, s), 2.7 (1 H, m), 3.46 (1 H, m), 3.83 (3 H, s), 5.47 (2 H, s), 6.87–7.3 (6 H, m).

Compounds **8a** and **7a** were not resolved on TLC (silica gel with various solvent systems).

Method B. A solution of **6** (0.1002 g, 0.54 mmol) and 0.1638 g (0.54 mmol) of **9** in 25 mL of acetonitrile was added via syringe

Scheme V



pump to a solution of 0.1638 g (0.54 mmol) of **9** in 10 mL of acetonitrile while, simultaneously, 0.8 mL (1.6 mmol) of a 40% aqueous solution of tetra-*n*-butylammonium hydroxide was added to the solution from another syringe pump. Addition was completed after 12 h. At the end of 48 h, the reaction mixture was filtered to remove the polyamide (53.4 mg), and the filtrate was evaporated to dryness. The residue (0.5351 g) contained a maximum of 88% **7a** plus **8a** (based on **9**) from an NMR of the crude mixture. The residue was subjected to column chromatography (silica, 20% ethyl acetate–80% hexanes) to provide 0.1 g of a mixture of **11** and **12** and 0.0906 g (0.22 mmol, 42%) of **7a** plus **8a** identical with that from method A.

4-Phenyl-2-azetidinone (15) was prepared by the method of Graf:[28] 22% yield; mp 98–102 °C (ethyl acetate–hexanes) (lit.[28] mp 108–109 °C); IR (CCl_4) ν_{CO} 1750 cm^{-1}; NMR δ 2.7–3.8 (2 H, m), 4.61–4.81 (1 H, dd, J = 2, 5 Hz), 6.65–7.2 (br s), 7.38 (5 H, s).

Methyl *p*-hydroxymandelate (16) was prepared by the method of Ladenburg et al.[29] without purification of intermediates in 24% yield overall from *p*-hydroxybenzaldehyde: mp 146–147 °C; IR (KBr) ν_{CO} 1724 cm^{-1}; NMR (acetone-d_6) δ 3.72 (3 H, s), 4.5 (br s, 1 H), 5.1 (2 H, br s), 6.8–7.4 (4 H, m); mass spectrum, m/e 182.

Attempted Quinone Methide Addition. Acid Catalysis. Compound **15** (0.1239 g, 0.84 mmol) and 0.1361 g (0.74 mmol) of **16** were dissolved in 5 mL of acetonitrile containing 100 mol % of trifluoroacetic acid. The reaction was followed by TLC, and the temperature was gradually increased to reflux. After 21 h at reflux, the reaction was cooled and evaporated in vacuo. Column chromatography (silica, 75% ethyl acetate–25% hexanes) yielded **16** (88.8 mg, 0.49 mmol, 66%), **15** (38.1 mg, 26 mmol, 31%), and **18** (19.6 mg, 0.08 mmol, 10%). For 3-[(trifluoroacetyl)-amino]-3-phenylpropionic acid (**18**): mp 153–155 °C dec; NMR (acetone-d_6) δ 3.0 (2 H, d), 5.4 (1 H, br s), 7.4 (5 H, s); mass spectrum (CI with isobutane), m/e 262 (M + 1); IR (KBr) ν_{CO} 1693, ν_{NH} 3350. Anal. Calcd for $C_{11}H_{10}NO_3F_3$: C, 50.57; H, 3.83; N, 5.36. Found: C, 50.77; H, 4.49; N, 5.41.

DDQ Oxidation of Methyl (*p*-Hydroxyphenyl)acetate (19). Compound **19** was prepared in 88% yield from (*p*-hydroxyphenyl)acetic acid with methanol–HCl; bp 112–116 °C (50 μmHg) [lit.[30] bp 158–159 °C (3 mmHg)]. Compound **21** (0.5 g, 3 mmol) in 20 mL of absolute methanol was treated with 0.69 g (3.1 mmol) of DDQ (Aldrich, recrystallized from dichloromethane). The solution immediately turned a deep purple. After 6 h the solution was evaporated to dryness and titurated with dichloromethane. H_2DDQ (0.51 g, 2.2 mmol, 71%) was isolated by filtration. The rest of the reaction mixture was chromatographed (silica, 50% ethyl acetate–50% hexanes). The first fraction yielded 0.29 g of a mixture of starting material and overoxidized products. The second fraction contained 0.22 g (1.1 mmol, 37%) of **20**: NMR δ 3.4 (3 H, s), 3.75 (3 H, s), 4.52 (1 H, s), 6.8–7.4 (6 H, m).

DDQ Oxidation of 19 Plus 15. Compounds **15** (0.5107 g, 3.5 mmol) and **19** (0.597 g, 3.6 mmol) dissolved in 20 mL of acetonitrile were treated with 0.80 g (3.5 mmol) of DDQ. After 12 h the reaction mixture was concentrated and chromatographed (silica, 50% ethyl acetate–50% hexanes). Compound **19** (61.4 mg, 0.36 mmol) was recovered along with 0.51 g (3.5 mmol, 100%) of **15**. The intervening fractions contained an uncharacterized adduct of **19** and H_2DDQ.

Glyoxylates 21 a–c. The glyoxylates employed were generated by either of two methods.

Method A. Grignard Addition to Dialkyl Oxalates.[18a] The appropriate *p*-alkoxy bromide (20 mmol) in 25 mL ether was added to 0.48 g (20 mmol) of Mg turnings in 25 mL of ether. After addition of EtMgI initiator, the reaction was heated at reflux until all the Mg had dissolved. When the mixture cooled, two layers formed. Both were added to 40 mmol of the dialkyl oxalate in 200 mL of ether at −78 °C. The reaction was warmed to room temperature after the addition and then refluxed for 15 min. The glyoxylate was isolated by distillation or chromatography after washing with aqueous NH_4Cl.

Method B. Oxidation of *p*-Alkoxymandelates. The *p*-alkoxymandelates were prepared according to the method of Ladenburg[29] from the corresponding *p*-alkoxybenzaldehyde. Oxidation was carried out by using Sarret's reagent. Thus, 5 mmol of the *p*-alkoxymandelate was added to 20 mmol of chromium trioxide in 20 mL of pyridine and the mixture stirred for 5 h at room temperature. The reaction mixture was added to 300 mL of ether and filtered. The ether layer was washed with 1.2 N HCl (4 × 50 mL), 50 mL of H_2O, and 50 mL of saturated NaCl and dried over $MgSO_4$. The product was purified by chromatography on silica gel.

***tert*-Butyl (*p*-methoxyphenyl)glyoxylate (21a)** was prepared in 44% yield by method A. The compound was isolated as an oil after silica gel chromatography: NMR δ 1.6 (9 H, s), 3.92 (3 H, s), 6.95–8.08 (4 H, m).

Benzyl [*p*-(benzyloxy)phenyl]glyoxylate (21c) was prepared by method B: 22% yield; mp 75.0–76.5 °C (ether–hexanes); NMR δ 5.12 (2 H, s), 5.38 (2 H, s), 6.9–8.08 (4 H, m), 7.43 (5 H, s). Attempted use of method A did not lead to **25c**; apparently the *p*-benzyloxy group interfered with the formation of the Grignard reagent.

Preparation of α-Diazo Esters.[18a] The (p-alkoxyphenyl)-glyoxylate (3 mmol) and 3 mmol of *p*-toluenesulfonylhydrazide (Aldrich) in 25 mL of anhydrous methanol were stirred for 15 h at room temperature and finally for 1 h at 65 °C. After evaporation of the solvent, the crude tosylhydrazone was added to a solution of 2 g (87 mmol) of Na in approximately 20 mL of ethylene glycol. The solution was heated to 70 °C for 5 min, cooled, and extracted with 100 mL of ether. This procedure was repeated three times. The combined ether extracts were washed with 25 mL of 0.05 N NaOH and 25 mL of saturated NaCl and dried over Na_2SO_4. After evaporation, the residue was recrystallized from ether–hexanes.

***tert*-Butyl (*p*-methoxyphenyl)-α-diazoacetate (22a)** was prepared in 64% yield as an orange oil that solidified on being cooled to −20 °C: NMR δ 1.58 (9 H, s), 3.8 (3 H, s), 6.8–7.5 (4 H, m).

Benzyl [*p*-(benzyloxy)phenyl]-α-diazoacetate (22c) was prepared in 83% yield: mp 97–101 °C dec; IR (CCl_4) 2175 (=N_2), 1700 (CO) cm^{-1}; NMR δ 5.1 (2 H, s), 5.32 (2 H, s), 6.9–7.5 (4 H, m), 7.42 (5 H, s).

Carbenoid Insertion. Compound **6** (0.5 mmol) and 0.002 mmol of rhodium(II) acetate (Alfa) were dissolved in 10 mL of dry benzene. The α-diazo ester (0.5 mmol) was added, and the solution was heated to 80 °C. Over a 2-h period, an additional 2 equiv of the α-diazo ester in 10 mL of benzene was added to the warm solution. Fifteen minutes after the final addition of diazo ester, the reaction was cooled, evaporated, and chromatographed. The isomeric ratio of the produces was determined by high-pressure LC, and the diastereomers were separated under similar conditions. Compounds **7a** and **8a** were prepared in this manner in 26% yield. The isomers were separated by high-

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(29) Ladenburg, K.; Folkers, K.; Major, R. T. *J. Am. Chem. Soc.* **1936**, *58*, 1292–1294.
(30) Testa, E.; Fontanella, L.; Christiani, G.; Gallo, G. *J. Org. Chem.* **1959**, *24*, 1928–1936.

pressure LC [Ultrasphere ODS-Si, 25 cm × 10 mm column, 5-μm particle size; eluent 4% isopropyl alcohol–96% hexanes at 5 mL/min]. The retention time of **7a** was 9.8 min, while that of **8a** was 12 min. The ratio of **7a** to **8a** was calculated to be 4:3. Compounds **7a** and **8a** prepared in this manner had identical physical properties with those isolated from PTC alkylations.

Compounds **7b** and **8b** were prepared in 60% yield in a 4:3 ratio as determined by high-pressure LC (Ultrasphere ODS, 25 cm × 4.6 mm; 65% methanol–35% H_2O, flow rate 1 mL/min; retention time for **7b**, 14 min, and for **8b**, 12.1 min). For **7b**: NMR δ 1.45 (9 H, s), 1.08–1.45 (3 H, t), 2.92–3.03 (2 H, dd, $J_{\beta\text{-H}}$ = 2 Hz), 3.82 (3 H, s overlapping a 1 H t), 4.0–4.4 (2 H, q), 4.8 (1 H, br), 5.3 (1 H, br d), 5.55 (1 H, s), 6.83–7.3 (4 H, m). For **8b**: NMR δ 1.40 (9 H, s), 1.08–1.45 (3 H, t), 2.5 (1 H, m), 3.5 (1 H, m), 3.82 (3 H, s), 4–4.4 (2 H, q), 4.8 (1 H, br), 5.3 (1 H br d), 5.55 (1 H, s), 6.8–7.3 (4 H, m).

Compounds **7c** and **8c** were prepared in 67% yield after chromatography on Florisil (gradient of ethyl acetate–hexanes). Analytical high-pressure LC (Ultrasphere ODS, 25 cm × 4.6 mm column, 72% methanol–28% H_2O, flow rate 1.5 mL/min) showed a ratio of **7c** (27.8 min) to **8c** (30 min) of 1:1.2. The diastereomers were separated by medium-pressure LC [Michel–Miller column packed with TLC grade silica gel; 98% hexanes–2% isopropyl alcohol, 100–150 psi].

For **8c** (oil): IR (CCl_4) 1760, 1720 cm^{-1}; NMR (XL-100) δ 1.43 (9 H, s), 2.97 (1 H, m), 3.46 (1 H, m), 4.85 (1 H, br m), 5.05 (2 H, s), 5.18 (2 H, s), 5.58 (1 H, s), 6.88–7.2 (4 H, m), 7.29 (5 H, s), 7.39 (5 H, s), carbamate NH obscured by the aromatic peaks; $[\alpha]^{25}$ +55.4 (*c* 1.2, CH_3OH).

For **7c** (oil): IR (CCl_4) 1760, 1720 cm^{-1}; NMR (XL-100) δ 1.39 (9 H, s), 3.01 (1 H, dd, *J* = 2 Hz), 3.90 (1 H, t), 4.92 (1 H, m), 5.05 (2 H, s), 5.17 (2 H, s), 5.59 (1 H, s), 6.88–7.2 (4 H, m), 7.28 (5 H, s), carbamate NH obscured by the aromatic peaks; $[\alpha]^{25}$ −77.8 (*c* 0.95, CH_3OH). Epimerization of **8c** was effected by stirring it at room temperature in neat Et_3N for 2 days. The new diastereomeric mixture contained **7c** and **8c** in a ratio of 4:3 (determined by high-pressure LC and NMR).

Deprotection of 3-ANA Derivatives. BBr_3 Cleavage of the *t*-Boc Group. The mixture of **7b** and **8b** (59.4 mg, 0.16 mmol) was dissolved in 5 mL of CH_2Cl_2 and cooled to −10 °C under nitrogen. BBr_3 (2 mL, Alfa) as a 1 M solution in CH_2Cl_2 was added dropwise. Compounds **7b** and **8b** disappeared immediately by TLC (50% ethyl acetate–50% hexanes). The reaction was allowed to warm to room temperature over 40 min. After repeated evaporations from methanol, the residue was examined by NMR (100 MHz); no *tert*-butyl groups were seen, but the ethyl ester [δ 1.24 (t), 4.3 (q)] and the methyl ether [δ 3.89 (3 H, s), δ 3.99 (3 H, s)] were still present. Upon treatment of the residue with BBr_3 in CH_2Cl_2/DMF at room temperature for 3 h, a product more polar than 3-ANA (high-pressure LC, Ultrasphere ODS, 99.5% H_2O *N* 0.5% MeOH) was formed.

NaI/Chlorotrimethylsilane Cleavage of *t*-Boc and *tert*-Butyl Esters. A mixture of **7c** and **8c** (67.5 mg, 0.13 mmol) in 4 mL of CH_3CN was treated with NaI (0.1246 g, 0.83 mmol) and Me_3SiCl (0.12 mL, 0.83 mmol) at room temperature for 24 h. After an aqueous workup, a solid residue was isolated that lacked only the *t*-Boc group by NMR. Repetition of the reaction at reflux led to cleavage of the benzyl groups in addition to the *t*-Boc group and the β-lactam as determined by high-pressure LC and NMR. Treatment of **7a** and **8a** with this reagent under room-temperature conditions cleaved the *tert*-butyl ester and *t*-Boc groups in less than 15 min. The methyl ether remained intact after being refluxed for 24 h.

Compound **23c** was prepared by dissolving **7c** (19 mg, 0.04 mmol) in 10 mL of ethyl acetate with *p*-toluenesulfonic acid monohydrate (7 mg, 0.04 mmol). After being stirred for 24 h, the reaction mixture was added to 5% $NaHCO_3$ (25 mL) and extracted with 100 mL of additional ethyl acetate. After the mixture was dried over $MgSO_4$ and evaporated, **23c** was isolated: 9.4 mg (0.023 mmol, 63%); $[\alpha]^{25}$ −78.2 (*c* 0.16, CH_3OH); NMR data identical with those previously reported.[3a]

Hydroxamates 27–30 and 2-azetedinones 31–34 were prepared by the previously reported method.[4a,b]

***O*-Pivaloyl 2,2′-dimethyl-3-hydroxypropiohydroxamate (27)** was isolated in 82% yield from the reaction of 2,2-dimethyl-3-hydroxypropionic acid (**25**)[30] and *O*-pivaloylhydroxylamine:[23] mp 124–124.5 °C (after recrystallization from ethyl acetate–hexanes); IR (CCl_4) 1700, 1760 cm^{-1}; NMR δ 1.25 (6 H, s), 1.33 (9 H, s), 3.58 (3 H, br m), 9.75 (1 H, 6 s); mass spectrum (CI with CH_4), *m/e* 218 (M + 1). Anal. Calcd for $C_{10}H_{19}O_4$: C, 55.30; H, 8.75; N, 6.45. Found: C, 55.06; H, 8.73; N, 6.50.

***O*-Pivaloyl *N*-α-(carbobenzyloxy)-L-serinehydroxamate (28)** was obtained in 86% yield: mp 78–80 °C (after recrystallization from CCl_4); IR (CCl_4) 1700, 1780 cm^{-1}; NMR δ 1.31 (9 H, s), 3.8 (3 H, br m), 4.5 (1 H, br m), 5.08 (2 H, s), 6.2–6.4 (1 H, br d), 7.3 (5 H, s), 7.3 (1 H, br s); mass spectrum (CI with CH_4), *m/e* 339 (M + 1); $[\alpha]^{20}_D$ −31.6 (*c* 2.095, CH_3OH). Anal. Calcd for $C_{16}H_{22}N_2O_6$: C, 56.80; N, 6.51; N, 8.28. Found: C, 56.57; H, 6.51; N, 8.45.

***O*-*tert*-Butyl *N*-α-(carbobenzyloxy)-L-serinehydroxamate (29)** was obtained in 88% yield by using *O*-*tert*-butylhydroxylamine hydrochloride (Fluka): mp 115–117 °C (ethyl acetate–hexanes); IR (KBr) 1660 cm^{-1}; NMR δ 1.27 (9 H, s), 3.8 (3 H, br m), 4.3 (1 H, br m), 6.1–6.3 (1 H, br d), 7.35 (5 H, s), 9.3 (1 H, br s); mass spectrum (CI with CH_4), *m/e* 311 (M + 1); $[\alpha]^{20}$ −30.1° (*c* 1.65, CH_3OH). Anal. Calcd for $C_{15}H_{22}N_2O_5$: C, 57.80; H, 7.02; N, 8.87. Found: C, 58.06; H, 7.10; N, 9.03.

***O*-(Triphenylmethyl) *N*-α-(carbobenzyloxy)-L-serinehydroxamate (30)** was obtained in 62% yield by using *O*-tritylhydroxylamine (Fluka): mp 133–135 °C (after recrystallization from ethyl acetate–hexanes); IR (KBr) 1670 cm^{-1}; NMR δ 3.6 (3 H, br m), 4.9 (1 H, br m), 5.42 (2 H, s), 7.1–7.4 (20 H, m), 7.1–7.4 (1 H, br m); mass spectrum (CI with CH_4), *m/e* 243 ($^+CPh_3$); $[\alpha]^{20}_D$ −25.3° (*c* 1.15, CH_3OH). Anal. Calcd for $C_{30}H_{28}N_2O_5$: C, 72.58; H, 5.64; N, 5.64. Found: C, 72.40; H, 5.46; N, 5.48.

3,3′-Dimethyl-1-(pivaloyloxy)-2-azetidinone (31) was obtained in 70% yield; mp 43–45 °C (after recrystallization from hexanes). The physical properties were identical with those reported.[4b]

3-[(Carbobenzyloxy)amino]-1-(pivaloyloxy)-2-azetidinone (32) was obtained in 71% yield: mp 113.5–114 °C (after recrystallization from ethyl acetate–hexanes); IR (CCl_4) 1815, 1775, 1730 cm^{-1}; NMR δ 1.3 (9 H, s), 3.58–3.68 (1 H, dd, *J* = 2.5 Hz), 3.87–4.0 (1 H, t, *J* = 5 Hz), 4.8 (1 H, br m), 5.15 (2 H, s), 5.97–6.17 (1 H, br d), 7.35 (5 H, s); mass spectrum (CI with CH_4), *m/e* 321 (M + 1); $[\alpha]^{20}_D$ +9.84 (*c* 2.215, CH_3OH). Anal. Calcd for $C_{16}H_{20}N_2O_5$: C, 60.0; H, 6.25; N, 8.75. Found: C, 60.16; H, 6.36, N, 8.74.

3-[(Carbobenzyloxy)amino]-1-*tert*-butoxy-2-azetidinone (33) was obtained in 63% yield: mp 79–80 °C (after recrystallization from ether–hexanes); IR (neat film) 1780, 1720 cm^{-1}; NMR δ 1.32 (9 H, s), 3.43–3.57 (1 H, dd, *J* = 2 Hz), 3.7–3.9 (1 H, t, *J* = 5 Hz), 4.5–4.75 (1 H, m), 5.1 (2 H, s), 7.52 (5 H, s); $[\alpha]^{20}_D$ −16.4 (*c* 2.21, CH_3OH). Anal. Calcd for $C_{15}H_{20}N_2O_4$: C, 61.64; H, 6.84; N, 9.59. Found: C, 61.43; H, 6.77; N, 9.37.

3-[(Carbobenzyloxy)amino]-1-(triphenylmethoxy)-2-azetidinone (34) was obtained in 56% yield: mp 120–125 °C; IR (CCl_4) 1780, 1730 cm^{-1}; NMR δ 2.75–3.0 (2 H, m), 4.0–4.4 (1 H, br m), 5.02 (2 H, s), 5.5–5.7 (1 H, br d), 7.1–7.6 (20 H, m).

Deprotection of Model Compound 31. Compound **31** (0.304 g, 1.53 mmol) was added to 20 mL of 50% aqueous methanol containing $(NH_4)_2CO_3$ (0.1257 g, 1.59 mmol) and Na_2CO_3 (0.95 g, 9.05 mmol). $TiCl_3$ (4.8 mL, 20% aqueous solution) was then added dropwise. After the addition, the pH was adjusted to 7.5 with Na_2CO_3. After another 1.5 h, the reaction mixture was extracted with 150 mL of ethyl acetate. After the organic layer was dried over $MgSO_4$, filtered, and evaporated, an NMR spectrum of the residue showed only **36**[4b,5] and pivalamide.

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Registry No. **3**, 3262-72-4; **4**, 26048-92-0; **5**, 71405-00-0; **6**, 72229-74-4; **7a**, 76529-90-3; **7b**, 76529-91-4; **7c**, 76529-92-5; **8a**, 76529-93-6; **8b**, 76529-94-7; **8c**, 76529-95-8; **9**, 27737-94-6; **10**, 76529-89-0; **11**, 76529-96-9; **12**, 76529-97-0; **15**, 5661-55-2; **16**, 68758-69-0; **18**, 21735-63-7; **19**, 14199-15-6; **20**, 76529-98-1; **21a**, 75716-84-6; **21b**,

40140-16-7; **21c**, 76529-99-2; **22a**, 76530-00-2; **22c**, 76530-01-3; **23c**, 67509-39-1; **25**, 4835-90-9; **27**, 76530-02-4; **28**, 76530-03-5; **29**, 76530-04-6; **30**, 76530-05-7; **31**, 71404-95-0; **32**, 76530-06-8; **33**, 76530-07-9; **34**, 76530-08-0; *p*-methoxyphenylacetic acid, 104-01-8; *p*-methoxyphenylacetyl chloride, 4693-91-8; *p*-hydroxybenzaldehyde, 123-08-0; (*p*-hydroxyphenyl)acetic acid, 156-38-7; *O*-pivaloylhydroxylamine, 35657-34-2; *O*-*tert*-butylhydroxylamine HCl, 39684-28-1; *O*-tritylhydroxylamine, 31938-11-1; *O*-benzylhydroxylamine, 622-33-3.

Oxidation of Hydrazines with Benzeneseleninic Acid and Anhydride[1a]

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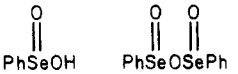
Benzeneseleninic acid (**1**) and anhydride (**2**) oxidize hydrazine or 1,2-disubstituted derivatives to the corresponding diazenes. Hydrazides afford selenoesters **4**, *N,N'*-diacyl- or -diaroylhydrazines **5**, and carboxylic acids. Benzeneselenenic acid (**7**) is a required intermediate in selenoester formation and may be generated independently by the reaction of triphenylphosphine with **1**. Selenoesters are efficiently prepared by the slow addition of a mixture of the hydrazide and triphenylphosphine to **1** in dichloromethane solution. Polar solvents are unsuitable. Inverse addition provides compounds **5** as the major products. Oxidation of hydrazides of structure HO-$(CH_2)_n$CONHNH$_2$ gives the corresponding selenoesters **14** and acids **16** when n = 11 or 14 and lactones **17** and **18** when n = 4 or 3. Arylhydrazines react with **1** or **2** to furnish arenes **23** and aryl phenyl selenides **24**.

Benzeneseleninic acid (**1**) and anhydride (**2**) are stable, readily available, odorless solids which serve as oxidants of diverse organic substrates. The latter include sulfur compounds,[2] nitrogenous species,[3] compounds containing hydroxyl[4] or carbonyl[3d,5] functions, and benzylic hydrocarbons.[5b] A number of synthetically useful transformations have resulted from these studies.

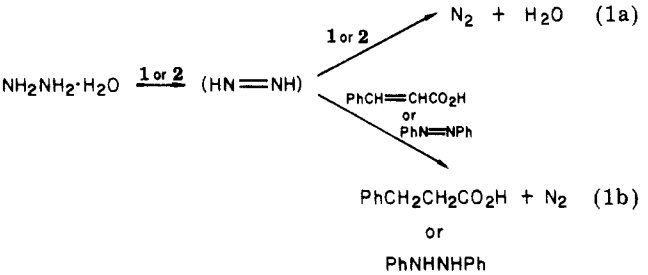


1 **2**

Recently, one of us observed that variously substituted hydrazines react vigorously with **1** or **2** at room temperature to produce diazenes or products derived from their fragmentation.[6] The dehydrogenation of hydrazo compounds to diazenes has been accomplished by numerous methods in the past.[7] However, limitations of scope and attendant side reactions frequently curtail their effectiveness. New methods for producing diazenes as products or as unstable intermediates (e.g., as in the case of monosubstituted derivatives) are therefore of continuing interest. In view of the rich and varied chemistry of species containing the -N=N- linkage, we performed the studies of hydrazine oxidations with **1** and **2** described herein.

Results and Discussion

Rheinboldt and Giesbrecht[8] observed that seleninic acids are reduced to selenenic acids (RSeOH) when treated with hydrazine hydrate, hydrochloride, or sulfate. We have found that an initial dehydrogenation produced diazene (diimide) when hydrazine hydrate was oxidized with **1** or **2**. Evidence for diazene formation derived from the in situ conversion of added azobenzene or cinnamic acid to *N,N'*-diphenylhydrazine or hydrocinnamic acid, respectively,[9] as shown in eq 1a,b. Since diazene may itself be easily



oxidized, its efficient generation requires the presence of excess hydrazine hydrate during the reaction. Under such conditions the oxidant reacts preferentially with the hydrazine. The oxidation of *N,N'*-diphenylhydrazine back to azobenzene (vide infra) is similarly avoided.

The reactions of two symmetrically disubstituted hydrazines with **1** or **2** were also studied. The oxidation of *N,N'*-diphenylhydrazine with **2** afforded azobenzene in 97% yield while *N,N'*-diisopropylhydrazine was converted to the corresponding diazene (azo compound) quantitatively by an equimolar amount of **1** or by 0.5 molar equiv of **2**. When 0.5 molar equiv of **1** were used in the oxidation, only a small amount (<10%) of the hydrazine remained

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