of Maryland, 1970.
(2) W. A. Henderson, Jr., and C. A. Streuli, *J. Am. Chem. Soc.*, **82**, 5791 (1960).
(3) H. Goetz and A. Sidhu, *Justus Liebigs Ann. Chem.*, **682**, 71 (1965).
(4) D. Seyferth, S. O. Grim, and T. O. Read, *J. Am. Chem. Soc.*, **83**, 1617 (1961).
(5) J. C. Sheldon and S. Y. Tyree, Jr., *J. Am. Chem. Soc.*, **80**, 2117 (1958).
(6) J. P. Day and L. M. Venanzi, *J. Chem. Soc. A*, 1363 (1966).
(7) W. McFarlane and R. F. M. White, *Chem. Commun.*, 744 (1969).
(8) (a) L. J. Vande Griend and J. G. Verkade, *J. Am. Chem. Soc.*, **97**, 5958 (1975); (b) L. J. Vande Griend and J. G. Verkade, *Phosphorus*, **3**, 13 (1973).
(9) G. A. Olah and C. W. McFarland, *J. Org. Chem.*, **36**, 1374 (1971).
(10) S. O. Grim and W. McFarlane, *Can. J. Chem.*, **46**, 2071 (1968).
(11) L. J. Vande Griend, J. G. Verkade, C. Jongsma, and F. Bickelhaupt, *Phosphorus*, **6**, 131 (1976).
(12) G. A. Olah and C. W. McFarland, *J. Org. Chem.*, **34**, 1832 (1969).
(13) S. O. Grim and A. W. Yankowsky, *Phosphorus Sulfur*, in press.
(14) M. van den Akker and F. Jellinek, *Recl. Trav. Chim. Pays-Bas*, **86**, 275 (1967).
(15) S. O. Grim, A. W. Yankowsky, S. A. Bruno, W. J. Bailey, E. F. Davidoff, and T. J. Marks, *J. Chem. Eng. Data*, **15**, 497 (1970).
(16) L. D. Quin and J. J. Breen, *Org. Mag. Reson.*, **5**, 17 (1973).
(17) H. Goetz, H. Juds, and F. Marschner, *Phosphorus*, **1**, 217 (1972).
(18) (a) D. Wittenberg and H. Gilman, *J. Org. Chem.*, **23**, 1063 (1958); (b) K. Issleib and H. O. Fröhlich, *Z. Naturforsch. B*, **14**, 349 (1959).

Synthesis of β,γ-Unsaturated Amino Acids

Jack E. Baldwin,* Stephen B. Haber, Carolyn Hoskins, and Lawrence I. Kruse

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

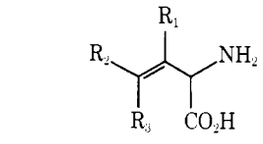
Received September 28, 1976

An efficient synthesis and resolution of the β,γ-unsaturated amino acid isodehydrovaline (Ia) is described. The same compound, as its D antipode, was also obtained by a selective degradation of penicillin V. A reasonably efficient synthesis of vinylglycine is reported in detail.

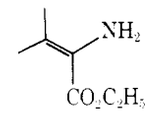
The β,γ-unsaturated amino acids, of the general structure I, are a growing class of natural products. These interesting substances possess potent biological activity,[1] both as enzyme inhibitors[2-4] and as antibiotics.[5] In connection with our interest in penicillin biosynthesis and synthesis[6] we have initiated studies on the synthesis of such compounds and here report these results in detail.

As a synthetic intermediate we required large amounts of the so far unknown substance Ia, which we have called isodehydrovaline, to distinguish it from the well-known α,β isomer, dehydrovaline ethyl ester (II).[7] Substance Ia is closely related to the fungal metabolites β-methylenenorvaline (Ib)[8] and β-methylenenorleucine (Ic).[9] Although a synthesis of Ib has been reported,[8] via a Strecker reaction on α-ethylacrolein, the low yield (0.4%) induced us to investigate alternative routes to Ia. We found that the intermediate in the synthesis of II, methyl α-nitrodimethylacrylate (III),[7] could be efficiently deconjugated by kinetic protonation of the potassium salt IV, yielding the β,γ-unsaturated isomer V, in greater than 90% isolated yield.[10] The success of this deconjugation may reside in the orthogonal and therefore nonconjugated nature of IV, resulting from steric hindrance, as shown in VI. This substance V was smoothly reduced and hydrolyzed in one step with tin and hydrochloric acid to the racemic amino acid Ia (45%). An efficient resolution of this amino acid (Ia) was accomplished by conversion to the chloroacetyl derivative (Schotten–Baumann) and selective deacylation of the L antipode by the use of hog acylase I. A reference sample of the D form of Ia was obtained in a reasonably efficient sequence from penicillin V. Thus conversion of the β-sulfoxide methyl ester of penicillin V, VII, to the known thiazoline VIII by the method of Cooper[11] (treating with trimethyl phosphite), followed by acid-catalyzed conversion to the thiazole IX, yielded thereby a dipeptide containing the intact D-isodehydrovaline unit. Selective hydrolysis of the amide bond was achieved by way of the iminochloride and methanolysis to give the methyl ester of D-isodehydrovaline hydrochloride as X (R = CH_3), which was hydrolysed with aqueous acid to the free amino acid hydrochloride (X, R = H), identical in all respects with that obtained by total synthesis.

A reported synthesis of the naturally occurring parent[12] of this class of β,γ-unsaturated amino acids, vinylglycine (Id),

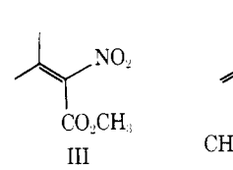


I

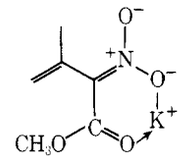


II

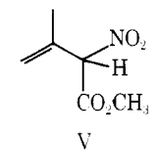
Ia, $R_1 = CH_3$; $R_2 = R_3 = H$
b, $R_1 = CH_2CH_3$; $R_2 = R_3 = H$
c, $R_1 = CH_2CH_2CH_3$; $R_2 = R_3 = H$
d, $R_1 = R_2 = R_3 = H$



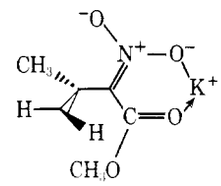
III



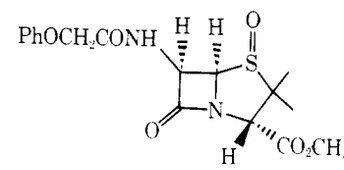
IV



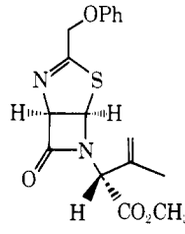
V



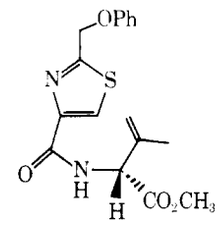
VI



VII



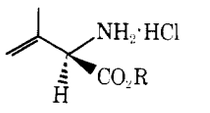
VIII

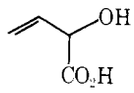


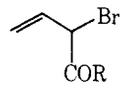
IX

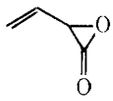
has proceeded in only modest yield.[1,4,13] We developed a more efficient route to the racemic Id which we report here. Thus 2-hydroxy-3-butenoic acid (XI), readily obtained from acrolein cyanohydrin,[14] was converted (phosphorus tribromide) to the α-bromoacyl bromide (XII, R = Br) which was hydro-

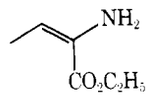
lyzed without isolation to the α-bromo acid (R = OH) and ammonolyzed to racemic vinylglycine (Id) in 29% overall yield. The success of this scheme depends upon the intermediacy of the bromo acid (XII, R = OH) which can be ammonolyzed relatively efficiently to Id, probably via the α-lactone XIII,


X


XI


XII


XIII


XIV

since all attempts to conduct ammonolysis on the ester (XII, R = CH_3CH_2O) led to very complex mixtures, mainly resulting from conjugation to XIV and then further reaction.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and have not been corrected. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. IR spectra were recorded on a Perkin-Elmer Model 700 spectrophotometer. NMR spectra were recorded on a Varian Associates T-60 spectrometer or a Hitachi Perkin-Elmer R-22B instrument. Silica gel for column chromatography was Davison Chemicals grade 950 (60–200 mesh) or Merck silica gel 60, no. 7734. Rotations were measured on a Perkin-Elmer 141 polarimeter.

Methyl 2-Nitro-3-methylbut-2-enoate (III). A solution of 660 mL of 90% fuming nitric acid and 96 mL of water was cooled to 0°C, and 200 g (1.75 mol) of methyl 3,3-dimethylacrylate was added over 1.25 h with vigorous stirring. The solution was stirred for 1.25 h at 0°C and 1 h at room temperature, then poured onto 3 L of crushed ice and extracted three times with 800 mL of chloroform. The chloroform extracts were combined and washed three times with 800 mL of water, six times with 600 mL of saturated $NaHCO_3$, and twice with 600 mL of brine, dried over $MgSO_4$, and concentrated. The residual oil was distilled to give 229 g (82%) of III as an almost colorless oil: bp 84–87°C (2.5 mm); IR (neat) 3000 (m), 1725 (s), 1650 (m), 1540 cm^{-1} (s); NMR ($CDCl_3$) δ 2.00 (s, 3 H), 2.29 (s, 3 H), 3.82 (s, 3 H).

Potassium Salt of Methyl 2-*aci*-Nitro-3-methylbut-3-enoate (IV). In a dry, N_2-flushed, 250-mL flask 4.01 g (0.1 mol) of ether washed potassium hydride was suspended in 50 mL of dry THF by vigorous stirring. The suspension was cooled to 0°C and a solution of 15.9 g (0.1 mol) of III in 20 mL of THF added over 1 h followed by an additional 50 mL of THF. After stirring at 0°C for 2 h the paste was filtered, washed three times with ether, and dried in vacuo to give 18.6 g (94.5%) of yellow crystals. A portion of the salt was recrystallized from methanol/ether to give analytically pure, thick, yellow prisms: mp 180–193°C dec; IR (KBr pellet) 2950 (m), 1670 (s), 1400 (s), 1345 (s), 1280 (s), 1200 cm^{-1} (s); NMR (D_2O) δ 1.96 (d, J = 2 Hz, 3 H), 3.77 (s, 3 H), 5.12 (m, 1 H), 5.25 (q, J = 2 Hz, 1 H).

Anal. Calcd for $C_6H_8NO_4K$: C, 36.53; H, 4.10; N, 7.10. Found: C, 36.37; H, 4.20; N, 7.03.

Methyl 2-Nitro-3-methylbut-3-enoate (V). A solution of 19.7 g (0.1 mol) of IV in 300 mL of water was stirred while 150 mL of 1 *N* HCl was added. The resulting oil was extracted three times with 100 mL of ether, and the extracts were combined, dried over $MgSO_4$, and concentrated to give 15.3 g (96%) of colorless oil, used directly without purification: IR (neat) 2950 (w), 1755 (s), 1650 (w), 1565 (s), 1440 cm^{-1} (m); NMR ($CDCl_3$) δ 1.96 (d, J = 2 Hz, 3 H), 3.90 (s, 3 H), 5.29 (broad singlet, 1 H), 5.40 (q, J = 2 Hz, 1 H), 5.68 (s, 1 H).

(±)-Isodehydrovaline Hydrochloride (Ia HCl). To 470 mL of concentrated HCl maintained at 50–65°C, 50 g (0.314 mol) of V was added in one portion, and 134 g (1.14 mol) of 20 mesh tin metal was added in small portions, with cooling to keep the temperature at 50–65°C. After the addition was complete, the mixture was heated to 100°C for about 50 min until all the tin had dissolved, then cooled and concentrated to dryness. The residue was dissolved in the minimum amount of water, saturated with H_2S, and filtered, the precipitated tin sulfides washed three times with water, and the filtrate concentrated to dryness. The residue was dried in vacuo of 60°C and, washed with dry acetone, then dry ether to give 27.05 g (57%) of amino acid hydrochloride: mp 206–208°C dec; IR (KBr pellet) 2800–3200 (s), 1720 (s), 1600 (s), 1490 (s), 1400 cm^{-1} (s); NMR (D_2O) δ 1.89 (d, J = 1 Hz, 3 H), 4.60 (s, 1 H, partly obscured by HOD), 5.33 (m, 2 H).

(±)-Isodehydrovaline (Ia). A solution of 6.08 g (40 mmol) of isodehydrovaline hydrochloride and 6.68 g (40 mmol) of silver acetate in 50 mL of water was warmed on a steam bath and shaken vigorously for 0.5 h, then cooled and allowed to stand for an additional 1 h. The precipitate was filtered and washed with water, and the combined filtrates were concentrated to give a light yellow powder which was recrystallized from water/ethanol to give 3.59 g (78%) of white microprisms: mp 212–215 °C dec; IR (KBr pellet) 2700–3100 (s), 2100 (w), 1580–1660 (s), 1360 cm^{-1} (s); NMR (D_2O) δ 1.79 (d, J = 2 Hz, 3 H), 4.24 (s, 1 H), 5.12 (broad singlet, 2 H). The amino acid was recrystallized from water/ethanol to give an analytical sample.

Anal. Calcd for $C_5H_9NO_2$: C, 52.15; H, 7.89; N, 12.17. Found: C, 51.97; H, 7.80; N, 12.12.

(±)-*N*-Chloroacetyl Isodehydrovaline. A solution of 4.6 g (40.6 mmol) of chloroacetyl chlorid in 17 mL of ether was added in small portions, alternately with 51 mL of 1 N sodium hydroxide, over the course of 15 min to a well-stirred ice-cold solution of 4.0 g (34.8 mmol) of isodehydrovaline in 35 mL of 1 N sodium hydroxide. After the addition was complete, the solution was stirred at 0 °C until the smell of acid chloride had disappeared, then acidified to pH 1 with concentrated hydrochloric acid and extracted five times with ether. The combined ether extracts were dried over $MgSO_4$ and concentrated to give a white, crystalline mass, which was recrystallized from ethyl acetate to give 3.26 g (51%) of fluffy white platelets: mp 117.5–119 °C; IR ($CHCl_3$) 2700–3600 (m), 3400 (m), 1730 (s), 1675 (s), 1500 cm^{-1} (m); NMR (acetone-d_6) δ 1.8 (d, J = 2 Hz, 3 H), 4.1 (s, 2 H), 4.9–5.15 (m, 3 H). The material was recrystallized from ethyl acetate to give an analytical sample.

Anal. Calcd for $C_7H_{10}NO_3Cl$: C, 43.88; H, 5.26; N, 7.31. Found: C, 43.65; H, 5.17; N, 7.31.

Resolution of Isodehydrovaline (Ia). A solution of 2.0 g (10.5 mmol) of chloroacetylisodehydrovaline in 80 mL of water was neutralized to pH 7.2 by the addition of 1 N ammonium hydroxide, 10 mg of hog acylase I (Sigma) added, and the solution allowed to stand for 24 h at 38 °C. The pH, which had dropped to 6, was readjusted to 7.2 by adding 1 N ammonium hydroxide, an additional 10 mg of enzyme added, and the solution allowed to stand at 38 °C for 24 h. The pH was adjusted to 7.2 again, a final 10-mg portion of enzyme added, and the solution allowed to stand overnight at 38 °C. The solution was adjusted to pH 5 with acetic acid, stirred with 150 mg of Norit, filtered, and concentrated to dryness below 40 °C. The residue was dissolved in the minimum amount of water and eluted slowly through a Dowex 50W-X4 column in the acid phase, followed by 200 mL of water. The eluent was concentrated to dryness below 40 °C to give 0.892 g of yellow crystals, which was recrystallized from ethyl acetate to give 0.629 g (63%) of D-*N*-chloroacetylisodehydrovaline as fluffy platelets: mp 126–129 °C; $[\alpha]^{27}D$ −97.1° (*c* 4.92, EtOAc). The crystals were heated with 12 ml of 2 N HCl at 100 °C for 1.5 h, and the solution concentrated and dried in vacuo at 80 °C to give a light yellow solid, which was triturated three times with dry ether, then dried in vacuo to give D-isodehydrovaline hydrochloride: mp 202–205 °C dec; $[\alpha]^{27}D$ −112° (*c* 3.44, H_2O). The amino acid hydrochloride was dissolved in a little water, the solution neutralized to pH 6 with 1 N lithium hydroxide and concentrated to dryness, and the residue recrystallized from water/ethanol to give 0.252 g (67%) of D-isodehydrovaline as microprisms, mp 210–213 °C dec, $[\alpha]^{27}D$ −165° (*c* 3.32, H_2O), constant to further recrystallization. The ion exchange column was eluted with 200 mL of 1 N hydrochloric acid, the eluent concentrated to dryness, and the residue dissolved in a little water. The pH was adjusted to 10 with 1 N LiOH, and the solution concentrated to dryness to remove ammonia. The residue was redissolved in a little water, the pH adjusted to 6 with 1 N hydrochloric acid, and the solution concentrated to dryness to give a white powder, which was recrystallized twice from water/ethanol to give 0.227 g (37.6%) of L-isodehydrovaline as microprisms, mp 212–215 °C dec, $[\alpha]^{27}D$ +165° (*c* 4.60, H_2O), constant to repeated recrystallizations. L-Isodehydrovaline hydrochloride was prepared by concentrating a solution of L-isodehydrovaline from 1 N hydrochloric acid, then drying in vacuo to give a white, crystalline salt: mp 201–204 °C dec; $[\alpha]^{27}D$ +113° (*c* 3.64, H_2O). Both enantiomers exhibit spectral properties identical with those of the racemic amino acid.

2-Phenoxymethyl-4-[(1*R*)-methoxycarbonyl-2-methyl-2-propenylaminocarbonyl]thiazoline (IX). A solution of methyl phenoxyacetamidopenicillinate 1-oxide (VII) (30 g, 79 mmol) and trimethyl phosphite (10 mL, 85 mmol) in 150 mL of dry benzene was heated to the reflux temperature under nitrogen for 40 h with Dean-

Stark removal of water. The solution was cooled, diluted with more benzene, washed with water and brine, dried ($MgSO_4$), and concentrated to give crude VIII as a dark oil: NMR ($CDCl_3$) δ 1.77 (br s, 3 H), 3.73 (s, 3 H), 4.83 (s, 1 H), 4.92 (br s, 3 H), 5.07 (d, J = ca. 1 Hz, 1 H), 5.90 and 5.96 (AB quartet, J_{AB} = 5 Hz, 2 H), 6.73–7.47 (m, 5 H).

A solution of crude VIII in 350 mL of methanol containing aqueous hydrochloric acid (1 N, 75 mL) was refluxed for 2 h. The cooled solution was diluted with methylene chloride, washed with water and brine, dried ($MgSO_4$), and concentrated. Column chromatography on silica gel (9:1 chloroform–ethyl acetate as eluent) gave IX as an oil in 55% overall yield from VII (15 g): IR ($CHCl_3$) 3375, 1735, 1665, 1600 cm−1; NMR ($CDCl_3$) δ 1.9 (d, J = ca. 1 Hz, 3 H), 3.82 (s, 3 H), 4.97–5.42 (m, 5 H; a 2 H singlet was visible at δ 5.35), 6.8–7.5 (m, 5 H), 8.00 (d, J = ca. 10 Hz, 1 H), 8.12 (s, 1 H).

In another experiment, methyl phenoxyacetate, from hydrolysis of the thiazoline ring, was isolated in 10% yield as an oil which crystallized on standing: IR ($CHCl_3$) 1740, 1600, 1500, 1100 cm−1; NMR ($CDCl_3$) δ 3.68 (s, 3 H), 4.55 (s, 2 H), 6.67–7.33 (m, 5 H); mp 97–100 °C.

Alternatively when 0.2 mL of water was added to VII (10 g, 26.4 mmol) and trimethyl phosphite (3 mL, 25.4 mmol) in 50 mL of benzene and the reaction conducted as for the preparation of VIII; IX was isolated in 67% yield (6.06 g) after dry column chromatography.

Cleavage of IX with Phosphorus Pentachloride. (−)-Isodehydrovaline Methyl Ester Hydrochloride (X, R = CH_3). To a stirred solution of IX (9.4 g, 27 mmol) in 60 mL of dry benzene under nitrogen was added phosphorus pentachloride (5.65 g, 27 mmol). After stirring for 2 h at room temperature, the reaction mixture was cooled in an ice bath and sequentially treated with 16 mL of cold, dry methanol containing 27 mmol of dry HCl and with 75 mL of cold methanol. After the reaction mixture had stirred for 30 min in the ice bath and 15 min at room temperature, 150 mL of 1 N aqueous HCl was added and stirring was continued overnight. The aqueous phase was separated, washed with methylene chloride, and evaporated to afford 3.67 g of a slightly yellow solid. Recrystallization from methanol–ether gave X (R = CH_3) as white crystals, 2.89 g (65%): mp 157–159.5 °C; IR (KBr) 1740, 1580, 1500 cm^{-1}; NMR (D_2O) δ 1.80 (d, J = ca. 1 Hz, 3 H), 3.80 (s, 3 H), 4.65 (shoulder on HOD peak, assigned s, 1 H), 5.20 (br s, 1 H), 5.27 (d, J = ca. 1 Hz, 1 H).

(−)-Isodehydrovaline Hydrochloride (X, R = H). A solution of X (R = CH_3) (160 mg, 0.97 mmol) in 16 mL of 6 N aqueous HCl was refluxed for 2 h and evaporated to give X (R = H): mp 205–207 °C dec; NMR (D_2O) δ 1.87 (d, J = ca. 1 Hz, 3 H), 4.62 (s, 1 H), 5.30 (m, 2 H); $[\alpha]^{23}D$ −95.3° (c 10.1, H_2O).

(±)-Vinylglycine (Id). To a stirred solution of 2-hydroxy-3-butenoic acid (XI, 7.7g, 75 mmol) in ether (20 mL) at 25 °C under nitrogen was added dropwise freshly distilled PBr_3 (15.4 g, 56.7 mmol) in ether (52 ml). After stirring for 24 h, H_2O (20 mL) was added dropwise and stirred for 15 min. The layers were separated and the aqueous layer extracted with ether (ca. 250 mL) which was concentrated to leave a yellow oil. After stirring with H_2O (10 mL) for 15 min, the oil was added dropwise to concentrated NH_4OH (275 mL) at 0 °C over 15 min. After addition was completed the reaction mixture was allowed to warm to room temperature and was stirred for 4 days.

The solvents were concentrated in vacuo to leave a yellow solid which was dissolved in H_2O (5 mL), adjusted to pH 6.5 (1 N NH_4OH), and chromatographed on a Dowex 50 × 4 cation exchange column (H^+ cycle). Concentration of the 1 N NH_4OH eluents left vinylglycine as a yellow solid, 1.93 g (26.2%): NMR (D_2O) δ 4.29 (d, J = 7 Hz, 1 H), 5.33–6.0 (complex multiplet, 3 H); IR (KBr) 2600–3200, 2080, 1600, 940 cm^{-1}.

Recrystallization from H_2O/ethanol gave a white powder, mp 218–220 °C dec (lit.[13] mp 216–218 °C dec).

Acknowledgments. We thank the National Science Foundation and the National Institutes of Health for financial support. One of us (L.I.K.) would like to thank Professor C. Walsh for helpful discussions.

Registry No.—(±)-Ia, 60049-36-7; (±)-Ia HCl, 61348-75-2; D-Ia, 60103-01-7; D-Ia HCl, 61348-76-3; L-Ia, 61376-23-6; L-Ia HCl, 61376-24-7; Id, 52773-87-2; III, 3536-09-2; IV K salt, 61363-52-8; V, 60049-37-8; VII, 10209-03-7; VIII, 59203-76-8; IX, 61348-77-4; (−)-X (R = CH_3) HCl, 61348-78-5; XI, 56525-48-5; nitric acid, 7697-37-2; methyl 3,3-dimethylacrylate, 924-50-5; (±)-*N*-chloroacetylisodehydrovaline, 61348-79-6; chloroacetyl chloride, 79-04-9; D-*N*-chloroa cetylisodehydrovaline, 61376-25-8; methyl phenoxyacetate, 2065-23-8.

References and Notes

(1) R. Rando, *Acc. Chem. Res.*, **8**, 281 (1975).
(2) I. Giovanelli, L. D. Owens, and S. H. Mudd, *Biochim. Biophys. Acta*, **227**, 671 (1971); L. D. Owens, J. F. Thompson, R. G. Pitcher, and T. Williams, *J. Chem. Soc., Chem. Commun.*, 714 (1972).
(3) R. Rando, *Nature (London)*, **250**, 586 (1974).
(4) R. Rando, *Biochemistry*, **13**, 3859 (1974).
(5) J. P. Scannell, D. L. Preuss, T. C. Demney, L. H. Sello, T. Williams, and A. Stempel, *J. Antibiot.*, **25**, 122 (1972); U. Sahm, G. Knoblock, and F. Wagner, *ibid.*, **26**, 389 (1973).
(6) J. E. Baldwin, M. A. Christie, S. B. Haber, and L. I. Kruse, *J. Am. Chem. Soc.*, **98**, 3045 (1976).
(7) M. Masaki, C. Shin, H. Kurita, and M. Ohta, *Chem. Commun.*, 1447 (1968); C. Shin, M. Masaki, and M. Ohta, *J. Org. Chem.*, **32**, 1860 (1967).
(8) B. Levenberg, *J. Biol. Chem.*, **243**, 6009 (1968).
(9) R. Vervier and J. Casimir, *Phytochemistry*, **9**, 2059 (1970).
(10) L. Bouveault and A. Wahl, *Bull. Soc. Chim. Fr.*, **25**, 800 (1901).
(11) R. D. G. Cooper and F. L. José, *J. Am. Chem. Soc.*, **92**, 2575 (1970).
(12) G. Dardenne, J. Casimir, M. Marlier, and P. O. Larsen, *Phytochemistry*, **13**, 1897 (1974).
(13) P. Friis, P. Helboe, and P. O. Larsen, *Acta Chem. Scand., Ser. B*, **28**, 317 (1974).
(14) J. W. E. Glattfield and R. E. Hoen, *J. Am. Chem. Soc.*, **57**, 1405 (1935).