Thioglycolic Acid Reduction.—A soution of N-benzyloxycarbonyl-L-methionyl sulfoxide L-asparaginyl-O-*t*-butyl-L-threonine *t*-butyl ester (0.095 g, 0.0015 mole) in dioxane (2 ml) and water (1 ml) was mixed with thioglycolic acid (0.105 ml, 5 equiv) and kept at 50° under a nitrogen atmosphere for 8 hr. The solution was evaporated, and the oily residue crystallized from aqueous methanol to produce compound VIII: mp 146–148°; $[\alpha]^{26}D$ −21.6° (*c* 1.00, methanol); R_f 0.53; identical infrared spectrum with an authentic sample.

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Amino Acids and Peptides. VI.[1] Synthesis of a Heptapeptide Sequence (A_{20}–A_{26}) of Glucagon

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During the past several years, various approaches to the synthesis of the A_{20}–A_{26} segment of the hyperglycemic hormone glucagon[2] have been elaborated in some detail. For example, N-*t*-butyloxycarbonyl-L-glutaminyl-L-asparaginyl-L-phenylalanyl-L-valyl-L-glutaminyl-L-tryptophan hydrazide,[3] a hexapeptide that spans the A_{20}–A_{25} region, was formed by an azide reaction of N-*t*-butyloxycarbonyl-L-glutaminyl-L-asparaginyl-L-phenylalanine hydrazide and L-valyl-L-glutaminyl-L-tryptophan benzyloxycarbonylhydrazide. The related A_{20}–A_{23} tetrapeptide N-trifluoroacetyl-L-glutaminyl-β-*t*-butyl-L-aspartyl-L-phenylalanyl-L-valine hydrazide was made by a N,N′-dicyclohexylcarbodiimide[4] coupling involving N-trifluoroacetyl-β-*t*-butyl-L-aspartic acid and L-phenylalanyl-L-valine benzyloxycarbonylhydrazide.[5] The tripeptide N-trifluoroacetyl-L-glutaminyl-L-tryptophanyl-L-leucine hydrazide, which covers the short A_{24}–A_{26} sequence, was obtained through a similar N,N′-dicyclohexylcarbodiimide condensation between N-trifluoroacetyl-L-glutamine and L-tryptophanyl-L-leucine *t*-butyloxycarbonylhydrazide.[6] Most recently, the A_{22}–A_{26} area has been encompassed by the two related pentapeptides, N-phthalyl-L-phenylalanyl-valyl-L-glutaminyl-L-tryptophanyl-L-leucine hydrazide and N-phthalyl-L-phenylalanyl-L-valyl-L-glutaminyl-L-tryptophanyl-L-leucine. The former compound was prepared by an azide reaction utilizing N-phthalyl-L-phenylalanyl-L-valine hydrazide and L-glutaminyl-L-tryptophanyl-L-leucine butyloxycarbonylhydrazide, while the latter product was constructed by a stepwise prolongation that began with L-leucine *t*-butyl ester.[7]

In continuation of our earlier work on protected subunits of glucagon, there is described here a preparation of a heptapeptide that constitutes the complete A_{20}–A_{26} sequence, N-benzyloxycarbonyl-L-glutaminyl-β-*t*-butyl-L-aspartyl-L-phenylalanyl-L-valyl-L-glutaminyl-L-tryptophanyl-L-leucine methyl ester (I). The synthesis began with a N,N′-dicyclohexylcarbodiimide condensation of N-benzyloxycarbonyl-L-tryptophan[8] and L-leucine methyl ester[9] to give the corresponding dipeptide, N-benzyloxycarbonyl-L-tryptophanyl-L-leucine methyl ester (II). The blocking N-benzyloxycarbonyl group of compound II was removed by hydrogenolysis, and the resulting amine (III) was treated with N-benzyloxycarbonyl-L-glutamine 2,4,5-trichlorophenyl ester[10] to form the tripeptide N-benzyloxycarbonyl-L-glutaminyl-L-tryptophanyl-L-leucine methyl ester (IV). The polypeptide chain of IV was then progressively lengthened in the same manner through four more amino acid residues by utilizing in turn N-benzyloxy-carbonyl-L-valine 2,4,5-trichlorophenyl ester,[10] N-benzyloxycarbonyl-L-phenylalanine 2,4,5-trichlorophenyl ester,[11] N-benzyloxycarbonyl-β-*t*-butyl-L-aspartic acid *p*-nitrophenyl ester,[12,13] and N-benzyloxycarbonyl-L-glutamine 2,4,5-trichlorophenyl ester.[10] The end product was the desired heptapeptide (I). This sequence compares favorably with the other synthetic procedures mentioned earlier, and has the additional merit of employing pure, crystalline activated ester intermediates, which have been widely used in recent years.[14]

Finally, an alternative route to N-benzyloxycarbonyl-β-*t*-butyl-L-aspartic acid *p*-nitrophenyl ester is described here, in addition to a preparation of the dipeptide N-benzyloxycarbonyl-β-*t*-butyl-L-aspartyl-L-phenylalanine methyl ester (XII). Attention is called to the fact that the β-*t*-butyl blocking group is easily seen in the infrared, with two bands found at about 1390 and 1370 cm^{-1}, the intensity of the latter being much greater.

Experimental Section[15]

N-Benzyloxycarbonyl-L-tryptophanyl-L-leucine Methyl Ester (II).—To a stirred solution of N-benzyloxycarbonyl-L-tryptophan (34.6 g, 0.105 mole)[8] in acetonitrile (400 ml) in an ice bath at −10° was added a freshly prepared solution of L-leucine methyl ester [obtained by treating L-leucine methyl ester hydrochloride (21.5 g, 0.109 mole)[9] with 50% potassium carbonate solution (40 ml) at 0°, extraction of the free ester with ether (three 100-ml portions), and drying the combined organic phases for a short period (Na_2SO_4)], followed by dropwise addition of N,N′-dicyclohexylcarbodiimide (22.7 g, 0.110 mole) in acetonitrile (50 ml). After 8 hr the bath was removed and the mixture was allowed to stand for 36 hr. The N,N′-dicyclohexylurea (21.0

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g, 85%) was removed and the solution was washed with 5% hydrochloric acid, 5% sodium bicarbonate solution, salt water, and dried (Na_2SO_4). Evaporation of the solvent gave an oil, which was crystallized twice from ethyl acetate–hexane and once from ether–hexane to afford white needles of N-benzyloxycarbonyl-L-tryptophanyl-L-leucine methyl ester (7.91 g, 63%): mp 114–116°; $[\alpha]^{25.8}D$ −28.0° (*c* 4.20, methanol); R_f 0.65; ν_{max} 3400 (NH), 2950 (CH), 1710 broad (C=O), 1650 and 1520 broad (CONH), 1250 broad (CO), and 738 and 693 (Ph) cm^{-1}; λ_{max} 275 sh mμ (ε 5920), 282, (6350), and 291 (5570).

Anal. Calcd for $C_{25}H_{31}N_3O_5$: C, 67.08; H, 6.71; N, 9.03. Found: C, 66.76; H, 6.54; N, 9.03.

N-Benzyloxycarbonyl-L-glutaminyl-L-tryptophanyl-L-leucine Methyl Ester (IV).—A stirred solution of N-benzyloxycarbonyl-L-tryptophanyl-L-leucine methyl ester (29.3 g, 0.0629 mole) in methanol (250 ml) containing a suspension of 10% palladium-on-carbon catalyst (3.0 g) was hydrogenated for 5 hr. The filtered solution was evaporated to yield oily L-tryptophanyl-L-leucine methyl ester (III, 20.3 g, 97%, R_f 0.37). The amine III was dissolved in ethyl acetate (100 ml) and was treated with N-benzyloxycarbonyl-L-glutamine 2,4,5-trichlorophenyl ester [25.0 g, 0.0545 mole, mp 174–175°, $[\alpha]^{25.3}D$ −16.3° (*c* 3.68, dimethylformamide)][10] in dimethylformamide (150 ml). After standing for 7 days at room temperature, the reaction was filtered to obtain some product; the mother liquor was diluted with ether (700 ml) to precipitate additional tripeptide. The combined solids were crystallized from methanol–water to give N-benzyloxycarbonyl-L-glutaminyl-L-tryptophanyl-L-leucine methyl ester (31.9 g, 99%): mp 198–201°; $[\alpha]^{23.8}D$ −23.4° (*c* 2.05, dimethylformamide); R_f 0.47; ν_{max} 3400 broad, 2950 (CH), 1710 broad (C=O), 1650 and 1520 broad (CONH), 1250 broad (CO), and 740 and 695 (Ph) cm^{-1}; λ_{max} 222 mμ (ε 44,900), 275 sh (5390), 282 (5890), and 290 (5150).

Anal. Calcd for $C_{31}H_{39}N_5O_7$: C, 62.72; H, 6.62; N, 11.80. Found: C, 62.76; H, 6.65; N, 11.84.

N-Benzyloxycarbonyl-L-valyl-L-glutaminyl-L-tryptophanyl-L-leucine Methyl Ester (VI).—A stirred suspension of N-benzyloxycarbonyl-L-glutaminyl-L-tryptophanyl-L-leucine methyl ester (18.1 g, 0.0340 mole) in methanol (600 ml) containing a suspension of 10% palladium-on-carbon catalyst (2.0 g) was hydrogenated overnight. The filtered solution was evaporated to yield oily L-glutaminyl-L-tryptophanyl-L-leucine methyl ester (V, 15.6 g, 100%, R_f 0.10). The amine V was dissolved in dimethylformamide (200 ml) and was treated with N-benzyloxycarbonyl-L-valine 2,4,5-trichlorophenyl ester [18.0 g, 0.0420 mole, mp 94.5–95.0°, $[\alpha]^{27.2}D$ −16.3° (*c* 1.16, dimethylformamide)].[10] After 2 days, the reaction was concentrated, and then poured into ether to precipitate N-benzyloxycarbonyl-L-valyl-L-glutaminyl-L-tryptophanyl-L-leucine methyl ester (19.0 g, 81%). The analytical sample was crystallized from dimethylformamide–methanol: mp 243–245°; $[\alpha]^{26.5}D$ −23.3° (*c* 2.14, dimethylformamide); R_f 0.20; ν_{max} 3350 broad, 2950 (CH), 1720 (C=O), 1660 and 1520 broad (CONH), 1230 broad (CO), and 735 and 695 (Ph) cm^{-1}; λ_{max} 220 sh mμ (ε 37,000), 276 sh (5680), 282 (6060), and 291 (5220).

Anal. Calcd for $C_{36}H_{48}N_6O_8$: C, 62.41; H, 6.98; N, 12.13. Found: C, 62.30; H, 7.19; N, 12.30.

N-Benzyloxycarbonyl-L-phenylalanyl-L-valyl-L-glutaminyl-L-tryptophanyl-L-leucine Methyl Ester (VIII).—A suspension of N-benzyloxycarbonyl-L-valyl-L-glutaminyl-L-tryptophanyl-L-leucine methyl ester (7.32 g, 0.0106 mole) and 10% palladium-on-carbon catalyst (0.70 g) in methanol (350 ml) was hydrogenated for 2 hr while warming the solution with a lamp. The filtered solvent was evaporated to yield oily L-valyl-L-glutaminyl-L-tryptophanyl-L-leucine methyl ester (VII, 5.66 g, 96%, R_f 0.10). The amine VII was redissolved by the addition of a solution of N-benzyloxycarbonyl-L-phenylalanine 2,4,5-trichlorophenyl ester [6.08 g, 0.0127 mole, mp 141–142°, $[\alpha]^{26.2}D$ −39.8° (*c* 1.08, dimethylformamide)][11] in dimethylformamide (100 ml) and the reaction was allowed to stand for 7 days. After removal of the solvent, the oily residue was solidified with ether (200 ml), collected, dried, and reprecipitated from hot methanol to give the product (7.80 g, 88%). The analytical sample of N-benzyloxycarbonyl-L-phenylalanyl-L-valyl-L-glutaminyl-L-tryptophanyl-L-leucine methyl ester was reprecipitated from dimethylformamide–methanol: mp 253–255°; $[\alpha]^{25.8}D$ −22.0° (*c* 1.00, dimethylformamide); R_f 0.37; ν_{max} 3450 broad, 2965 (CH), 1720 broad (C=O), 1655 and 1520 broad (CONH), 1230 broad (CO), and 745 and 700 (Ph) cm^{-1}; λ_{max}^{MeOH} 221 sh (ε 43,750), 275 sh (5300), 282 (5730), and 290 (5100).

Anal. Calcd for $C_{45}H_{57}N_7O_9$: C, 63.34; H, 6.84; N, 11.67. Found: C, 63.86; H, 6.44; N, 11.67.

N-Benzyloxycarbonyl-β-*t*-butyl-L-aspartyl-L-phenylalanyl-L-valyl-L-glutaminyl-L-tryptophanyl-L-leucine Methyl Ester (X).—A suspension of N-benzyloxycarbonyl-L-phenylalanyl-L-valyl-L-glutaminyl-L-tryptophanyl-L-leucine methyl ester (1.68 g, 0.0020 mole) in methanol (200 ml) was heated to boiling, a mixture of palladium-on-carbon catalyst (0.183 g) in methanol (10 ml) was added, and the hot solution was allowed to cool as it was hydrogenated for 3 hr. The filtered solution was evaporated to yield as a colorless glass, L-phenylalanyl-L-valyl-L-glutaminyl-L-tryptophanyl-L-leucine methyl ester (IX, 1.64 g, >100%, R_f 0.12). The amine IX was redissolved in dimethylformamide (15 ml), N-benzyloxycarbonyl-β-*t*-butyl-L-aspartic acid *p*-nitrophenyl ester (1.07 g, 0.0024 mole)[12–14] was added, and the solution stood at room temperature for 5.5 days. A further portion of the active ester (0.103 g, 0.00010 mole) was introduced, and the solution was warmed at 50° for 1 hr, then heated to 70°, and ether (200 ml) was slowly added with swirling to precipitate the crude product. After standing for several hours at 0°, the material was filtered off, washed with ether and petroleum ether (bp 30–60°), dried, and crystallized from methanol to afford as a white powder N-benzyloxycarbonyl-β-*t*-butyl-L-aspartyl-L-phenylalanyl-L-valyl-L-glutaminyl-L-tryptophanyl-L-leucine methyl ester (1.22 g, 61%): mp 235–237°; $[\alpha]^{26.7}D$ −29.8° (*c* 1.01, dimethylformamide); R_f 0.57; ν_{max} 3320 broad, 2960 (CH), 1720 broad (C=O), 1660 and 1520 broad (CONH), 1390 and 1370 (*t*-butyl), 1230 broad (CO), and 740 and 695 (Ph) cm^{-1}; λ_{max}^{MeOH} 217 sh mμ (ε 35,500), 274 sh (4770), 282 (6090), and 291 (4380).

Anal. Calcd for $C_{53}H_{76}N_8O_{12}$: C, 62.95; H, 6.98; N, 11.08. Found: C, 62.80; H, 6.97; N, 11.29.

N-Benzyloxycarbonyl-L-glutaminyl-β-*t*-butyl-L-aspartyl-L-phenylalanyl-L-valyl-L-glutaminyl-L-tryptophanyl-L-leucine Methyl Ester (I).—A suspension of N-benzyloxycarbonyl-β-*t*-butyl-L-aspartyl-L-phenylalanyl-L-valyl-L-glutaminyl-L-tryptophanyl-L-leucine methyl ester (0.507 g, 0.00050 mole) in methanol (250 ml) was heated to boiling, a mixture of 10% palladium-on-carbon catalyst (0.105 g) in methanol was added, and the hot solution was allowed to cool as it was hydrogenated for 3 hr. The filtered solution was evaporated to leave solid β-*t*-butyl-L-aspartyl-L-phenylalanyl-L-valyl-L-glutaminyl-L-tryptophanyl-L-leucine methyl ester (XI, 0.477 g, >100%, R_f 0.15). This material was dissolved in dimethylformamide (7.0 ml), N-benzyloxycarbonyl-L-glutamine 2,4,5-trichlorophenyl ester (0.284 g, 0.00060 mole) was added, and the reaction was allowed to proceed at room temperature for 5.5 days. After warming the solution to 50° for 1 hr, the product was precipitated by gradually adding ether (200 ml), and after standing overnight, the gelatinous material was filtered, washed with ether and hexane, and air dried. The crude N-benzyloxycarbonyl-L-glutaminyl-β-*t*-butyl-L-aspartyl-L-phenylalanyl-L-valyl-L-glutaminyl-L-tryptophanyl-L-leucine methyl ester was obtained from dimethylformamide–methanol as a white solid (0.265 g, 43%): mp 239–240°; $[\alpha]^{25.8}D$ −32.3° (*c* 1.00, dimethylformamide); R_f 0.20; ν_{max} 3300 broad, 2960 (CH), 1720 sh (C=O), 1660 and 1520 broad (CONH), 1392 and 1368 (*t*-butyl), 1230 broad (CO), and 740 and 697 (Ph) cm^{-1}; λ_{max}^{MeOH} 217 sh, 275 sh, 282, and 291 mμ (ε values not calculated owing to insolubility of the heptapeptide).

Anal. Calcd for $C_{58}H_{78}N_{10}O_{14}\cdot 1DMF$: C, 60.43; H, 7.07; N, 12.72. Found: C, 60.37; H, 6.84; N, 12.46.

N-Benzyloxycarbonyl-β-*t*-butyl-L-aspartic Acid *p*-Nitrophenyl Ester.—Sodium hydroxide solution (1 *N*, 13.0 ml, 0.013 mole) was added with stirring to a solution of N-benzyloxycarbonyl-β-*t*-butyl-L-aspartic acid α-*p*-nitrobenzyl ester [5.97 g, 0.00013 mole, mp 94–95°, $[\alpha]^{25.5}D$ −17.4° (*c* 1.03, methanol)][16] in dioxane (13 ml). After stirring for 20 min at room temperature, the now homogeneous solution was diluted with water (100 ml) and extracted with ether. The aqueous phase was acidified with aqueous citric acid and extracted with ethyl acetate. The combined organic phases were washed with water, dried (Na_2SO_4), and evaporated to give a clear oil of N-benzyloxycarbonyl-β-*t*-butyl-L-aspartic acid (4.70 g, >100%, R_f 0.57);[16–18] dicyclohexylammonium salt, mp 126.5–128.5° (lit.[16,18] mp 124°, 126.5°). The crude acid and *p*-nitrophenol (1.81 g, 0.0013 mole) were

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dissolved in ethyl acetate (25 ml) and chilled to 0° by an ice bath. N,N'-Dicyclohexylcarbodiimide (2.68 g, 0.013 mole) in ethyl acetate (25 ml) was added, and the mixture was stirred for 1 hr at 0°, and then at room temperature overnight. The N,N'-dicyclohexylurea (2.69 g, 92%) was removed and the filtrate was evaporated to give an oil, which solidified on seeding and was crystallized from diisopropyl ether–ethyl acetate–hexane to afford long, almost colorless needles of N-benzyloxycarbonyl-β-*t*-butyl-L-aspartic acid *p*-nitrophenyl ester (4.90 g, 85%): mp 86.5–87.5°; $[\alpha]^{27.0}D$ +1.5° (*c* 1.00, chloroform); $[\alpha]^{27.0}D$ −32.8° (*c* 1.98, methanol); R_f 0.84; ν_{max} 2970 (CH), 1770 and 1700 broad (C=O), 1515 broad (CONH), 1387 and 1367 (*t*-butyl), 1160 (CO), and 742 and 697 (Ph) cm^{-1}; λ_{max} 268 mμ (ε 9720) [lit.[12,13] mp 86°; $[\alpha]^{20}D$ +3° (*c* 3, chloroform); infrared spectrum identical with that of an authentic specimen[14]].

N-Benzyloxycarbonyl-β-*t*-butyl-L-aspartyl-L-phenylalanine Methyl Ester (XII).—To a stirred solution of N-benzyloxycarbonyl-β-*t*-butyl-L-aspartic acid (1.18 g, 0.0036 mole) in acetonitrile (25 ml) was added L-phenylalanine methyl ester hydrochloride (0.935 g, 0.0043 mole), followed by triethylamine (0.493 g, 0.0043 mole). The solution was cooled to −5° by an ice–salt bath, then N,N'-dicyclohexylcarbodiimide (0.763 g, 0.0037 mole) in acetonitrile (5.0 ml) was added, and the reaction was allowed to stand at 4° for 18 hr, followed by 28 hr at room temperature. The N,N'-dicyclohexylurea (0.624 g, 75%) was removed, the solution was evaporated, and the residue was partitioned between ethyl acetate and water. The organic phase was washed with water, aqueous citric acid, water, sodium bicarbonate solution, water, and brine, and dried (Na_2SO_4). On removal of the solvent, the oily residue was redissolved in ether, filtered, and reevaporated to give an oil, which was allowed to stand under hexane in the cold room for 2 months. At this time, the solidified material was crystallized from ethyl acetate–petroleum ether (bp 30–60°) to afford colorless needles of N-benzyloxycarbonyl-β-*t*-butyl-L-aspartyl-L-phenylalanine methyl ester (1.15 g, 66%): mp 77–78°; $[\alpha]^{25.5}D$ −26.0° (*c* 1.00, methanol); R_f 0.85; ν_{max} 3395 (NH), 2975 (CH), 1720 broad (C=O), 1670 and 1525 broad (CONH), 1395 and 1368 (*t*-butyl), 1160 (CO), and 745 and 698 (Ph) cm^{-1}; λ_{max} 248 mμ (ε 273), 252 (363), 257 (418), 264 (341), and 267 (227).

Anal. Calcd for $C_{25}H_{30}N_2O_7$: C, 63.81; H, 6.43; N, 5.95. Found: C, 64.01; H, 6.79; N, 6.02.

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Nucleotides. VI.[1] Conversion of a Ribonucleoside to a Bis(ribonucleoside 5'-)carbonate[2]

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Ribonucleosides in which the ribose moiety bears a single blocking group on the 5' hydroxyl are frequently required as intermediates for syntheses.[3] Blocking groups which have been introduced directly and selectively at the 5' position are restricted to the acid-labile trityl (or methoxy-substituted trityl)[4] and 1''-methoxyisopropyl[5] groups; in addition, the alkali-labile acetyl group has been introduced at the 5' position by acidic treatment of a 5'-O-acetyl-2',3'-O-isopropylidene or benzylidene nucleoside[6,7] and also by hydrolysis of a 2',3',5'-tri-O-acetyl nucleoside.[7,8] The present communication describes a facile, two-step conversion of a ribonucleoside to a bis(ribonucleoside 5'-)carbonate. This novel type of 5'-monosubstituted ribonucleoside should be a useful intermediate for syntheses since it is stable under acidic conditions but readily regenerates the free nucleoside under mildly basic conditions.

Recent work[1] has shown that inosine and adenosine can be converted in high yield to the corresponding 2',3'-cyclic carbonates by acid-catalyzed alcohol interchange reactions with 1.2 to 1.5 molar equiv of diphenyl carbonate in dimethylformamide solution. These conversions are analogous to the formation of 2',3'-O-isopropylidene nucleosides by acid-catalyzed alcohol interchange reactions between ribonucleosides and 1 to 2 molar equiv of 2,2-diethoxypropane in dimethylformamide.[9] In these latter reactions, when a large (80-fold) excess of ketal and little or no acid are employed, ribonucleosides can react selectively at the 5' position to form 5'-O-1''-alkoxyalkyl derivatives.[5] Attempts to obtain 5'-O-phenoxycarbonylinosine in analogous fashion, *i.e.*, by use of a large excess of diphenyl carbonate, have, however, given as the primary product only inosine 2',3'-carbonate (**4**) (Table I). Attempted preparation of bis(inosine 5'-)carbonate (**3**) directly from inosine (I) and 0.7 molar equiv of diphenyl carbonate likewise furnished only inosine 2',3'-carbonate (**4**). However, reaction of inosine under more vigorous conditions with 2.0 molar equiv of diphenyl carbonate afforded bis(inosine 2',3'-carbonate 5'-)carbonate (**2**) in 70% yield. The ultraviolet absorption spectra of this compound at pH 2 and 12 were closely similar to those of inosine,[10] indicating absence of substitution on the purine ring. It is known[11] that organic five-membered cyclic carbonates show carbonyl absorption near 1800 cm^{-1}, whereas six-membered and acyclic carbonates absorb near 1760 cm^{-1}. In accord with its proposed structure, compound **2** exhibited maxima at both 1810 cm^{-1} and 1740 cm^{-1}; the spectrum of inosine 2',3'-carbonate,[1] on the other hand, lacks the maximum at 1740 cm^{-1}. The absence in compound **2** of a periodate–oxidizable (*i.e.*, unsubstituted) *cis*-diol system and the characterization of its hydrolysis product **3** (Scheme I) allow unequivocal assignment of the structure of **2**.

Compund **2** was heated at 100° in aqueous buffer, pH 8.0, when paper chromatography indicated that initially a single product was formed and that subsequently this underwent hydrolysis to inosine. The half-lives of **2** and the initial hydrolysis product were approximately 6 min and 35 min, respectively (Table II). The product of partial hydrolysis was isolated

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