heating it under reduced pressure, and the residue was chromatographed on grade IV alumina. Prolonged elution of the column with Skelly B solvent caused the development of a yellow band, which slowly passed into the filtrate. The excess of the solvent was evaporated from the filtrate, and an orange-yellow, oily substance separated. This slowly crystallized when the solution was allowed to stand for a few hours at room temperature. After filtration, 0.2 g of yellow 2-(3,4-dihydro-1-isoquinolyl)-5-phenylpyrrole (XIV), mp 113–114°, was obtained, as identified by its infrared spectrum.

5. **Dehydrogenation of 2-(3,4-Dihydro-1-isoquinolyl)-5-phenylpyrrole (XIV).**—A mixture of 0.3 g of 2-(3,4-dihydro-1-isoquinolyl)-5-phenylpyrrole and 0.05 g of 10% palladium-on-charcoal catalyst was heated at 180–200° under a slow stream of nitrogen for 45 min. The reaction mixture was taken up in 10 ml of boiling benzene, and the catalyst was removed by filtration. The excess of benzene was evaporated, and hot Skelly B solvent was added to the residue. By slow cooling, crystallization took place. After filtration, a yellow, crystalline solid was obtained which was recrystallized once from Skelly B solvent to give 0.2 g of 2-(1-isoquinolyl)-5-phenylpyrrole (VII), mp 140–141°. A mixture melting point test of this compound with a sample of the 2-(1-isoquinolyl)-5-phenylpyrrole obtained by the condensation of acrylonitrile with 1-cyano-2-benzoyl-1,2-dihydroisoquinaldonitrile (I) and the subsequent steps described previously showed no depression. The infrared spectra of the two compounds were identical also.

Acknowledgment.—This investigation was supported in part by a research grant (CA-06620) from the National Cancer Institute of the National Institutes of Health, Public Health Service. The nmr spectra were taken on a Varian A-60 apparatus, the purchase of which was made possible by a research instrument grant by the National Science Foundation to the University of Massachusetts.

The Nuclear Magnetic Resonance Spectra of the Enol Acetates and Ethers of Methylcyclopentanetriones and -diones. Homoallylic Spin Coupling

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The observation of homoallylic coupling (CH_3—C=C—CHR) through five bonds provides a convenient diagnostic method for elucidating the structures of enol ethers and acetates derived from 3-methyl-1,2-cyclopentanedione, 2-methyl-1,3-cyclopentanedione, 2-methyl-1,3,4-cyclopentanetrione, and related derivatives.

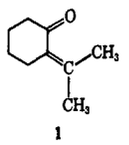
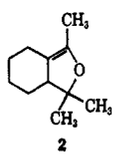
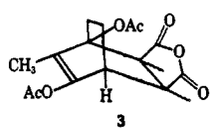
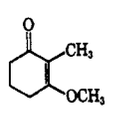
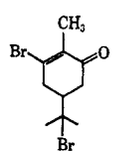
During the course of another investigation the problem arose of differentiating between isomeric enol acetates and enol ethers derived from unsymmetrically substituted 2-methyl-1,3-cyclopentanediones. The report following describes the successful application of nmr spectroscopy to this problem.

The term "homoallylic coupling" embraces those spin–spin interactions which occur between protons symmetrically disposed about a carbon–carbon double bond (CH—C=CCH).[1-3] The magnitude of this coupling lies in the range of 0–5 cps and is remarkably large in view of the five bonds which are involved. The geometry about the double bond, the conformation(s) adopted by the proton(s) with respect to the double bond, and the electron density at the double bond influence the magnitude of the homoallylic coupling constant.

trans, five-bond interactions are somewhat larger (*ca.* 0.5 cps) than *cis*, five-bond interactions.[4] This difference is clearly seen in the spectrum of 2-isopropylidenecyclohexanone (**1**)[5] (see Table I) where one of the vinyl methyl groups appears as a sharp triplet due to coupling with the *trans*-methylene group, while the other appears as a broad singlet due to smaller coupling with the same, but in this instance, *cis*-homoallylic methylene group. The appearance of a doublet vinyl methyl signal for vinyl ether **2** can also be attributed to spin coupling with the *trans*-homoallylic methine proton. Strong coupling with the *cis*-homoallylic methylene group would have produced a triplet or a complex multiplet.

TABLE I

MISCELLANEOUS COMPOUNDS SHOWING HOMOALLYLIC COUPLING

	CH_3 C=C (J, cps)
 **1**	1.77, broad singlet 1.92 t (~1.0)
 **2**	1.62 d (broadened) (~1.3)
 **3**	1.68 s
	1.71 t (~1.0)
	1.87 t (~1.0)

(1) E. E. Van Tamelen, S. H. Levin, G. Brenner, J. Wolinsky, and P. E. Aldrich, *J. Am. Chem. Soc.*, **81**, 1666 (1959).

(2) *Cf.* N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964, pp 110–113, and references cited therein.

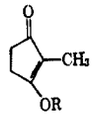
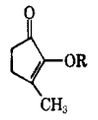
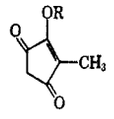
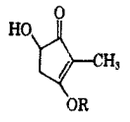
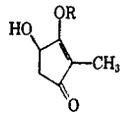
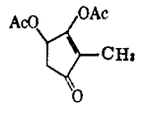
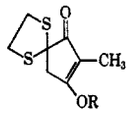
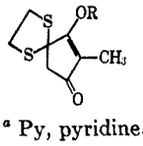
(3) S. Sternhell, *Rev. Pure Appl. Chem.*, **14**, 15 (1964).

(4) R. R. Fraser, *Can. J. Chem.*, **38**, 549 (1960); W. F. Beach and J. H. Richards, *J. Org. Chem.*, **26**, 3011 (1961).

(5) J. Wolinsky, M. Senyek, and S. Cohen, *ibid.*, **30**, 3207 (1965).

TABLE II

NMR SPECTRA OF CYCLOPENTANEDIONES AND THEIR DERIVATIVES

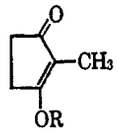
Compd	R (no.)	Solvent	CH_3 (J, cps)	CH_2	CH_3CO	CH_3O
	H (4a)	Py[a]	1.88 (t, 0.9)[c]	2.48		
	Ac (4b)	Py	1.65 (t, 2.0)	2.25–2.85	2.20	
		CCl_4	1.55 (t, 1.95)[c]		2.25	
	CH_3 (4c)	CCl_4	1.52 (t, 2.0)	2.12–2.82		3.94
	H (5a)	Py	2.00 (s)	2.30 (s)		
	Ac (5b)	Py	1.85 (s)	2.32 (s)	2.23	
		CCl_4	1.97 (s)	2.48 (m)	2.23	
	CH_3 (5c)	Py	1.84 (s)	2.21 (s)		3.89
		CCl_4	1.91 (s)	2.2–2.5		3.86
	H (6a, 7a)	Py	2.02 (t, ~1.0)	3.03 (m)		
		DMSO[b]	1.78 (t, ~1.0)	2.84 (m)		
	Ac (6b)	CCl_4	1.91 (s)	2.94 (s)	2.34	
	CH_3 (6c)		1.86 (s)	2.83 (s)		4.30
	CH_3 (13c)	Py	1.71 (t, 2.0)	2.4–3.28		3.82
	H (11)	Py	1.89 (s)	2.4–3.3		
	CH_3 (14c)	Py	1.80 (s)	2.4–3.28		4.24
	Ac (12)	$CDCl_3$	1.70 (d, ~2.0)	2.1–3.20	2.25	
		CCl_4	1.64 (d, ~2.0)			
	Ac (9b)	CCl_4	1.64 (t, ~2.0)	3.2–3.8	2.26	
	CH_3 (9c)	CCl_4	1.52 (t, ~2.0)	3.0–4.0		3.98
	H (8)	Py	1.86 (t, ~2.0)[c]	3.35–3.85		
	Ac (10b)	CCl_4	1.56 (s)	3.2–3.8	2.28	
	CH_3 (10c)	CCl_4	1.88 (s)	3.0–4.0		4.20

[a] Py, pyridine. [b] DMSO, dimethyl sulfoxide. [c] Measured at a sweep width of 50 cps.

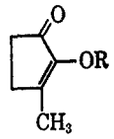
The concept of σ,π overlap has been advanced[6] to explain the dependence of J(homoallylic) on the angle subtended by the proton(s) with respect to the plane of the double bond. An angle of 90° should provide for the maximum observable coupling since the π orbitals will be able to interact maximally with the σ orbital of the C—H bond. Conversely, an angle of 0° should effectively reduce this interaction and the coupling constant should approach zero. The observation that the bicyclic enol acetate **3** shows no evidence for homoallylic coupling (the half-width of the vinyl methyl signal is the same as that of the acetate methyl groups) is consistent with this interpretation.

Finally, removal of electron density from the intervening double bond may cause a decrease in the coupling constant by effectively damping the medium through which the coupling occurs.[3]

Examination of the nmr spectra of diketones **4**[7] and **5** and their respective enol acetates **4b** and **5b** and enol methyl ethers **4c** and **5c** (see Table II) further demonstrates the utility of homoallylic coupling as a probe for structure elucidation.



4



5

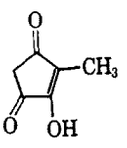
a. R = H
b, R = Ac
c, R = CH_3

The vinyl methyl group of 2-methyl-1,3-cyclopentanedione (**4a**) appeared as a slightly asymmetrical triplet in pyridine, with a coupling constant of 0.9 cps, while that of 3-methyl-1,2-cyclopentanedione (**5a**)[8] appeared as a singlet.[9] The enol acetates **4b** and **5b**,

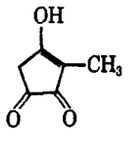
(6) *Cf.* ref 3, especially section 2, and references cited therein.
(7) C. B. C. Boyce and J. S. Whitehurst, *J. Chem. Soc.*, 2022 (1959).
(8) J. Bredenberg, *Acta Chem. Scand.*, **13**, 1733 (1959).
(9) In pyridine the diketones probably exist as the hydrogen-bonded enol forms **4a** and **5a** and to some extent as the corresponding ionized enolate anions.

prepared from the parent diketones by treatment with acetic anhydride, exhibited a triplet [J(homoallylic) = 1.95 cps] and a singlet methyl vinyl signal, respectively. The enol ethers **4c** and **5c** displayed the same behavior. Thus, the presence of a CH_3—C=C—CH_2 moiety in a 2-methyl-2-cyclopentenone system is characterized by the appearance of appreciable homoallylic coupling (~2 cps).

2-Methyl-1,3,4-cyclopentanetrione (**6**), prepared from diethyl oxalate and 2-butanone,[10] exhibited a triplet vinyl methyl signal, J = 1.0 cps, in DMSO, pyridine, D_2O, and $CDCl_3$. It is reported[11] that the addition of acid to a deuterium oxide solution of **6** had a negligible effect on this coupling constant, while addition of triethylamine to a deuteriochloroform solution caused an increase to 1.1 cps. The absence of a significant change in the spectrum was attributed to the existence of the tautomeric species **6a** and **7a** in rapid equilibrium.



6a



7a

Treatment of triketone **6** with isopropenyl acetate–p-toluenesulfonic acid or acetic anhydride–pyridine afforded a single enol acetate derivative. A negative response to a periodate test, the absence of color and lack of absorption[12] above 310 mμ, and the presence of three sharp singlets in its nmr spectrum demonstrated conclusively that the enol acetate was correctly represented by **6b**. Triketone **6** reacted with diazomethane to give a single methyl ether which was assigned structure **6c** since it showed a singlet vinyl methyl signal in its nmr spectrum.

The triketone **6** gave a monothioketal derivative **8** when kept with slightly more than 1 equiv of ethanedithiol.[13] The structure of **8** was established by its nmr spectrum [J(homoallylic] = 0.95 cps] and by Raney nickel desulfurization to 2-methyl-1,3-cyclopentanedione (**4a**). The thioketal **8** was converted to a mixture of enol acetates **9b** and **10b** with acetic anhydride–pyridine, while with diazomethane a mixture of enol ethers **9c** and **10c** was obtained. These mixtures were not separated, but were analyzed directly by nmr spectroscopy. In each case the nmr spectrum exhibited both a triplet and a singlet vinyl methyl resonance, as well as a pair of acetate and methoxy methyl signals.

Catalytic reduction of triketone **6** over platinum oxide gave 4-hydroxy-2-methyl-1,3-cyclopentanedione (**11**)[10] in addition to diketone **4a**. When treated with isopropenyl acetate, **11** afforded a single diacetate derivative (**12**) which exhibited a doublet vinyl methyl resonance. The reaction of **11** with diazomethane produced a mixture of **13c** and **14c** which was partially separated by fractional crystallization. The isomer displaying a triplet vinyl methyl resonance was assigned the structure **13c** containing a homoallylic methylene group.

(10) M. Orchin and L. W. Butz, *J. Am. Chem. Soc.*, **65**, 2296 (1943).
(11) J. A. Elvidge and R. Stevens, *J. Chem. Soc.*, 2251 (1965).
(12) *Cf.* C. Sandris and G. Ourisson, *Bull. Soc. Chim. France*, 350 (1958).
(13) L. F. Fieser, *J. Am. Chem. Soc.*, **76**, 1945 (1954).

An interesting feature of the spectra of the enol methyl ethers is the low field, 3.86–4.30 ppm, found for the methoxy signal. The largest downfield shifts are exhibited by compounds where the methoxy group is flanked by carbonyl, hydroxyl, or thioketal groups. This phenomenon is probably due to a combination of anisotropic and inductive effects.

The chemical shift of a methyl α to a carbonyl falls in the region between 1.52 and 1.71 ppm, while a methyl β to a carbonyl resonates downfield between 1.84 and 1.97 ppm. In the few examples examined it appears that a change from carbon tetrachloride to pyridine as solvent shifts an α-methyl to higher field and a β-methyl to lower field.

Experimental Section[14]

3-Acetoxy-2-methyl-2-cyclopentene-1,4-dione (**6b**).—A solution of 8 g (0.063 mole) of 2-methyl-1,3,4-cyclopentanetrione, prepared in 25% yield as described by Orchin and Butz[10] (mp 118–119.5°; $\lambda_{max}^{CCl_4}$ 5.65, 5.8, and 5.9 μ; nmr signals at 2.02 and 3.03 ppm), a few crystals of p-toluenesulfonic acid, and 20 ml of isopropenyl acetate was refluxed for 20 hr. Distillation *in vacuo* gave 7.8 g (74%) of the enol acetate **6b**: bp 103–106° (0.5 mm); $n^{18.5}D$ 1.4998–1.5000; infrared absorption at 5.6, 5.75, 5.8, and 6.0 μ; λ_{max}^{EtOH} 242.5 mμ (ϵ 12,200) and 311 mμ (ϵ 930). The oil slowly solidified and was recrystallized from hexane–benzene, mp 50.5–51°.

Anal. Calcd for $C_8H_8O_4$: C, 57.14; H, 4.80. Found: C, 56.94; H, 4.56.

The reaction of **6b** with o-phenylenediamine gave a high-melting solid (>295°) whose infrared spectrum was similar to the spectrum of the adduct obtained directly from the triketone **6**.

3-Methoxy-2-methyl-2-cyclopentene-1,4-dione (**6c**).—An ether solution of 1.23 g (0.01 mole) of triketone **6** was treated with an excess of diazomethane in ether. The ether was removed under diminished pressure to afford an oil which solidified. Recrystallization from hexane–benzene gave 938 mg (82%) of **3** and 170 mg of unreacted triketone **6**. Sublimation of a sample of the methyl ether **6c** gave a sample which showed mp 47.5–48° (lit.[15] mp 51°); infrared peaks at 5.7, 5.85, and 6.1 μ.

Anal. Calcd for $C_7H_8O_3$: C, 60.00; H, 5.75. Found: C, 60.11; H, 5.77.

4-Hydroxy-2-methyl-1,3-cyclopentanedione (**11**).—This compound was obtained in 51% yield by the catalytic reduction of **6** hydrate according to the procedure described by Orchin and Butz[10] and exhibited mp 161–165° (lit.[10] mp 166.8–168.2°), ν_{max} 6.4 μ.

3,4-Diacetoxy-2-methyl-2-cyclopenten-1-one (**12**).—A solution of 280 mg (0.0022 mole) of hydroxy ketone **11** and a few crystals of p-toluenesulfonic acid in 5 ml of isopropenyl acetate was refluxed for 20 hr. The excess reactants were removed under diminished pressure and the residual oil was crystallized from hexane–chloroform to give 126 mg of crude **12**, mp 71–74.5°. Two recrystallizations from hexane–chloroform gave a pure sample of **5**: mp 77.5–78°; λ_{max} 5.6, 5.7, 5.8, and 6.0 μ.

Anal. Calcd for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70. Found: C, 56.49; H, 5.61.

The mother liquors from the crystallization of **12** were combined, the solvent was evaporated, and the residue was subjected to vpc analysis. A second component, present to the extent of 20–30%, was collected and shown to be identical with acetate **4b** and presumedly arose from 2-methyl-1,3-cyclopentanedione (**4a**) which was a contaminant of **11**.

Enol Ethers 13c and 14c.—Enol ethers **13c** and **14c** were prepared in the manner described by Orchin and Butz.[10] Fractional crystallization of the product from benzene gave a crude separation of the two enol ethers. The least soluble isomer (mp 158–161°) was assigned structure **13c** on the basis of the presence of a triplet methyl signal at 1.73 ppm. The more soluble isomer, mp 74–78° (lit.[10] mp 85–86.4°), was assigned structure **14c** since it exhibited a singlet methyl signal at 1.80 ppm.

(14) All boiling and melting points are uncorrected. Nmr spectra were determined with a Varian Associates A-60 spectrometer. Chemical shifts are given in ppm downfield with tetramethylsilane as an internal reference. Microanalyses were performed by Dr. C. S. Yeh and associates.
(15) O. Diels, J. Sielisch, and E. Muller, *Ber.*, **39**, 1336 (1906).

2-Methyl-1,3,4-cyclopentanetrione 4-Monothioketal (8).—To a stirred solution of 1.5 g (0.012 mole) of triketone **6** and 1.21 g (0.015 mole) of ethanedithiol in 20 ml of glacial acetic acid was added 0.5 ml of boron trifluoride etherate. After 24 hr the solid was removed by filtration and washed well with ether. Recrystallization from benzene gave 1.75 g (73%) of **8**, mp 199–201° dec, with infrared peaks at 5.95 and 6.15 μ.

Anal. Calcd for $C_8H_{10}O_2S_2$: C, 47.49; H, 4.98. Found: C, 47.39; H, 5.25.

Raney Nickel Desulfurization of 8.—A solution of 240 mg of **8** in 10 ml of absolute alcohol was refluxed for 67 hr with a large excess of Raney nickel. The mixture was worked up in the usual manner to give, after recrystallization from water, 30 mg of diketone **4a** which was identified by its infrared and nmr spectra.

Enol Acetates 9b and 10b.—The monothioketal **8** was treated with acetic anhydride and pyridine according to the procedure described earlier. Upon molecular distillation there was obtained a light yellow oil which showed infrared peaks at 5.6, 5.8, and 6.0 μ. Nmr analysis of this liquid indicated the presence of **9b** and **10b** in a ratio of 2:1.

Enol Ethers 9c and 10c.—This mixture of enol ethers was prepared by the action of diazomethane on the diketone **9**. Evaporative distillation at 100° (0.5 mm) gave an oil which showed infrared peaks at 5.8 and 6.1 μ. Nmr analysis showed that the enol ethers **9c** and **10c** were present in a ratio of 2.4:1.

2-Acetoxy-3-methyl-2-cyclopenten-1-one (5b).—This compound was prepared according to the method described by Erickson and Collins[16] and showed mp 61.5° (lit.[16] mp 62–62.5°); λ_{max} 5.6, 5.8, and 6.0 μ.

(16) J. L. E. Erickson and F. E. Collins, *J. Org. Chem.*, **30**, 1050 (1965).

2-Methoxy-3-methyl-2-cyclopenten-1-one (5c).[17]—A mixture of 6 g (0.053 mole) of diketone **5a**, 6.75 g of dimethyl sulfate, and 3.19 g of sodium methoxide in 50 ml of dry methanol was refluxed for 46 hr. The mixture was cooled, poured into 150 ml of 5% sodium hydroxide solution, and extracted with ether. Distillation gave 3.8 g (57%) of **5c**; bp 33° (0.5 mm), $n^{25}D$ 1.4866, λ_{max} 5.8 and 6.0 μ.

3-Acetoxy-2-methyl-2-cyclopenten-1-one (4b).—A solution of 2.3 g of diketone **4a** (mp 201–205°), 5 ml of acetic anhydride, and 7 ml of pyridine was kept at room temperature for 17 hr and then distilled to give 2.6 g (84%) of the acetate **4b**: bp 66–67.5° (0.5 mm); $n^{14}D$ 1.4912; λ_{max} 5.6, 5.8, and 6.0 μ.

Anal. Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54. Found: C, 62.00; H, 6.76.

3-Methoxy-2-methyl-2-cyclopenten-1-one (4c).—A solution of 201 mg of diketone **4a** in ether–ethanol was treated with an excess of ethereal diazomethane. The solvents were removed and two sublimations *in vacuo* gave a solid: mp 61.8–62.3°, λ_{max} 5.85 and 6.1 μ.

Anal. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 66.65; H, 7.90.

2-Methyl-3-methoxy-2-cyclohexenone.—A slurry of 500 mg (0.0035 mole) of 2-methyl-1,3-cyclohexanedione in 100 ml of ether was treated with excess ethereal diazomethane. After stirring for 3 hr, the ether was evaporated and the yellow residue (570 mg) was purified by vpc (200°, 20% DEGS on Chromosorb) to afford the enol ether which showed ν_{max} (film) 5.85 and 6.25 μ, and nmr signals at 1.72 (triplet, vinyl methyl), 1.80–2.78 [multiplets, $(CH_2)_3$], and 3.87 ppm (singlet, OCH_3).

(17) M. A. Gianturco and P. Friedel, *Tetrahedron*, **19**, 2039 (1963).

Deuterated Amino Acids. III. Synthesis of DL-Aspartic-2,3,3-d_3 Acid, L-Glutamic-2,3,3,4,4-d_5 Acid, L-Asparagine-2,3,3-d_3, and L-Glutamine-2,3,3,4,4-d_5[1,2a]

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Highly deuterated asparaginyl and glutaminyl derivatives were prepared for use in the synthesis of certain deuterio analogs of oxytocin and the vasopressins. DL-Aspartic-2,3,3-d_3 acid (96.7% D) was obtained in 59% yield in a five-step synthetic sequence from acetic acid-d_4 *via* alkylation of phthalimidomalonic ester with ethyl bromoacetate-d_2. DL-Glutamic-2,3,3,4,4-d_5 acid as well as the d_9 acid (98.6 and 96.4% D, respectively) were synthesized in an eight-step sequence from dipotassium acetylenedicarboxylate (50% over-all) *via* alkylation of acetamidomalonic ester with ethyl β-bromopropionate-d_4. Pure L-glutamic-2,3,3,4,4-d_5 acid (96.4% D) was obtained by selective enzymatic deacylation of the N-acetyl derivative of the aforementioned DL-galutamic acid-d_9 in 85% yield. DL-Asparagine-2,3,3-d_3 was prepared in 68% over-all yield from DL-aspartic acid-d_7 deuteriochloride *via* ammonolysis of the β-methyl ester. Selective enzymatic deacylation of the corresponding N-acetyl derivative produced L-asparagine-2,3,3-d_3 (97.5% D) in 87% yield. DL-N-Acetyl glutamine-2,3,3,4,4-d_5 was synthesized in 85% yield in a three-step synthetic sequence from DL-glutamic acid-d_9 deuteriochloride *via* ammonolysis of the corresponding N-acetyl γ-methyl ester. Enzymatic deacylation afforded L-glutamine-2,3,3,4,4-d_5 (65%, 96.1% D).

With the general objective of providing highly deuterated amino acids as possible tools for use in the study of a variety of chemical and biological systems, as outlined briefly in a recent article,[1a] useful syntheses of the title compounds have been accomplished. More specifically, the deuterated asparaginyl and glutaminyl compounds are of interest in the synthesis of certain deuterio analogs of the peptide hormones, oxytocin, and the vasopressins. It is possible that study of a number of such analogs may provide information relative to the problem of structure and biological activity.

The syntheses presented in this report are useful in the sense that they are suitable for obtaining, in quantity, high yield, and isotopic purity, the title amino acids from relatively inexpensive materials. Further, these syntheses are considered to be the most satisfactory ones possible on the basis of our present knowledge,[3] including scouting experiments carried out in this laboratory.

DL-Aspartic-2,3,3-d_3 Acid.—Synthesis of this deuterated amino acid was best accomplished as outlined in

(1) (a) Part II: A. T. Blomquist, R. J. Cedergren, B. F. Hiscock, S. L. Tripp, and D. N. Harpp, *Proc. Natl. Acad. Sci. U. S.*, **55**, 453 (1966); (b) part I: A. T. Blomquist, B. F. Hiscock, and D. N. Harpp, *J. Org. Chem.*, **31**, 338 (1966).

(2) (a) This study was supported in part by the National Science Foundation, Grant No. G-18902; (b) National Institute of Health Molecular Biology Training Grant Predoctoral Fellow, 1965–1966; abstracted in part from the Ph.D. thesis of B. F. Hiscock, submitted to Cornell University in 1966; (c) National Institute of Health Molecular Biology Training Grant Postdoctoral Fellow, 1965–1966.

(3) (a) L-Aspartic-2,3,3-d_3 acid and L-glutamic-2,3,3,4,4-d_5 acid, among others, have been prepared by the hydrolysis of an alga grown in deuterated media: M. I. Blake, H. L. Crespi, V. Mohan, and J. J. Katz, *J. Pharm. Sci.*, **50**, 425 (1961); (b) J. S. Stekol and W. H. Hamill, *J. Biol. Chem.*, **120**, 531 (1937); N. Tamiya and T. Shimanouchi, *Spectrochim. Acta*, **18**, 895 (1962). L-Aspartic-2,3,3-d_3 acid has been prepared by these methods of exchange: (c) A. Murray, III, and D. L. Williams, "Organic Syntheses with Isotopes," Interscience Publishers, Inc., New York, N. Y., 1958; (d) J. P. Greenstein and M. Winitz, "Chemistry of the Amino Acids," Vol. 3, John Wiley and Sons, Inc., New York, N. Y., 1961.