in position 6,[14] and at a reduced rate since an equilibrium will exist between the two enols, which will favor the Δ^7 isomer. The small difference between the tertiary bromination of the 6-ketone and secondary bromination of the 7-ketone must be due to the fact that the Δ^6 double bond, in contrast to a Δ^5 double bond, introduces little strain in ring A. The 7- position is unique in its steric environment. An 11-ketone gives normally a 9-bromo derivative[15a] and $\Delta^{9(11)}$-enol acetate,[14, 15b] since approach to the underside of the molecule is not hindered.

EXPERIMENTAL

Ketones. These were highly purified specimens which had been prepared in a previous study.[1]

Solvents. Acetic acid (Baker Analyzed) was refluxed with and fractionated from chromium trioxide and acetic anhydride, and the fraction boiling at 107–108°/580 mm. was used. Acetic acid (1.8 l.) was diluted with distilled water to 2 l. and the solvent had d_4^{25} 1.0487. Hydrogen chloride, generated from analytical grades of hydrochloric and sulfuric acids, was passed into a portion of this acetic acid solution to give a 0.6171*M* solution. The hydrogen chloride was determined by adding aliquots to dilute nitric acid containing excess silver nitrate and titrating the excess silver nitrate with potassium thiocyanate. Bromine (Baker Analyzed) was added to the hydrochloric-acetic acid solution to about 0.05*M*. Its concentration was determined before each experiment, as described below.

A weighed quantity of ketone (0.2–0.3 g.) was dissolved in 90% acetic acid (*ca.* 80 ml.) in a 100 ml. graduated flask and allowed to equilibrate in temperature in a constant temperature bath maintained at 25.0 ± 0.1°. Ten milliliters of the stock solution of bromine were added and the volume quickly made up to the mark. Aliquots were withdrawn at various times and added to excess potassium iodide in water (*ca.* 20 ml.). The liberated iodine was titrated with sodium thiosulfate (0.05*M*), using starch as indicator.[16] Each experiment was repeated 3 or 4 times, and the rate constants for the first order reaction were obtained graphically. Linear plots were obtained up to about 60% reaction, but showed divergencies after this due to the catalytic action of the hydrogen bromide formed in the reaction, and to polybromination.[17]

Acknowledgments. This work was supported by grants from the Rockefeller Foundation, New York.

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(14) A similar steric effect has been suggested to explain the course of enol acetate formation. A. Crawshaw, H. B. Henbest, and E. R. H. Jones, *J. Chem. Soc.*, 731 (1954).

(15) (a) H. B. Henbest, E. R. H. Jones, A. A. Wagland, and T. I. Wrigley, *J. Chem. Soc.*, 2477 (1955); (b) D. H. R. Barton, R. M. Evans, J. C. Hamlet, P. G. Jones and T. Walker, *J. Chem. Soc.*, 747 (1954).

(16) *Cf.* D. P. Evans, *J. Chem. Soc.*, 785 (1936).

(17) Cholestan-3-one has been shown to absorb about 3 moles of bromine during one day, followed by uptake of a fourth in 5 days. D. H. R. Barton, J. F. McGhie, M. K. Pradhan, and S. A. Knight, *J. Chem. Soc.*, 876 (1955).

[CONTRIBUTION FROM THE LABORATORIES OF G. D. SEARLE AND COMPANY]

4,5-Epoxy-3-oxo Steroids

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Several 3-keto-Δ^4 steroids have been converted to the corresponding epoxides. Both the α and the β epoxides of progesterone were isolated.[2] Fermentation of 4,5-epoxypregnane-3,20-dione (I) by *Rhizopus nigricans* led to the isolation of 4β,5-epoxy-11α-hydroxypregnane-3,20-dione. Treatment of I with formic acid gave 4-hydroxyprogesterone (IV).[3]

As the preliminary step to investigating a hypothesis[4] that biological 11β-hydroxylation proceeds through the 4,5-epoxy-3-oxo steroid, a number of the 4,5-epoxides were prepared and a few of their reactions studied.[5]

The epoxides were prepared by alkaline hydrogen peroxide oxidation of the corresponding conjugated ketones. Table I summarizes the analytical data and physical constants of these oxides. Plattner, Heusser, and Kulkarni[6] have shown that 4-

(1) Present address: American Chemical Society Applied Journals, Chicago.

(2) W. Cole and P. L. Julian [*J. Org. Chem.*, 19, 131 (1954)] described an epoxide of progesterone, m.p. 173–175°, but gave no optical rotation or details of its synthesis.

(3) H. Levy and M. L. Mednick (private communication) have independently isolated 4-hydroxyprogesterone as a by-product from the reaction of progesterone with hydrogen peroxide and osmium tetroxide and also by the acid dehydration of the 4,5-diol.

(4) The hypothesis is that formation of the 4,5-epoxide is followed by an "anomalous" opening of the oxide involving a C_{11} hydrogen. The possibility of this type of opening is suggested by the work of A. C. Cope, S. W. Fenton, and C. F. Spencer [*J. Am. Chem. Soc.*, 74, 5884 (1952)]. The resulting 4,11-dihydroxy compound then dehydrates to give the 3-keto-Δ^4-11-hydroxy compound.

(5) (a) B. Camerino, B. Patelli, and A. Vercellone have recently [*J. Am. Chem. Soc.*, 78, 3540 (1956)] described the epoxides from testosterone and the cleavage products from these oxides. (b) Since the completion of our work other groups have reported on overlapping work. See B. Camerino and B. Patelli, *Il Farmaco* (Pavia), *Ed. sci.*, 11, 579 (1956); B. Camerino, B. Patelli, A. Vercellone, and F. Media, *Il Farmaco* (Pavia), *Ed. sci.*, 11, 586 (1956); and H. J. Ringold, E. Batres, O. Mancera, and G. Rosenkranz, *J. Org. Chem.*, 21, 1432 (1956).

(6) Pl. A. Plattner, H. Heusser, and A. B. Kulkarni, *Helv. Chim. Acta*, 31, 1822 (1948).

TABLE I

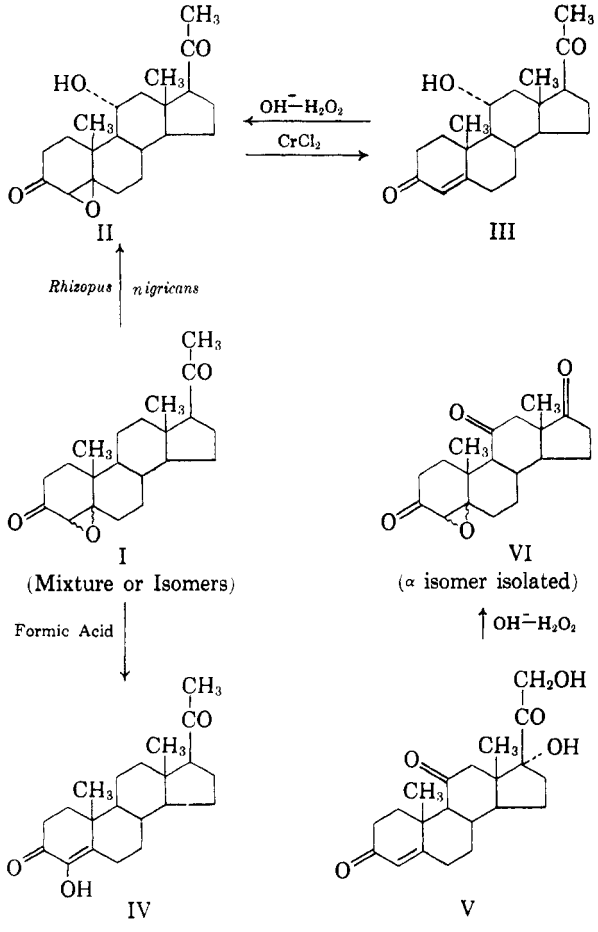
4,5-EPOXY-3-OXO STEROIDS

Starting Material	Product-epoxide isomer	Empirical Formula	M.P., °C.	$[\alpha]_D$	ΔM_D[a]	C Calcd.	C Found	H Calcd.	H Found	Recrystallized from
Adrenosterone	α	$C_{19}H_{24}O_4$	252° d.	+70°	−563°	72.13	72.10	7.65	7.69	Chloroform + methanol
	Second crop		195–225°	+190°	−189°		72.18		7.18	Acetone
4-Androstene-3,17-dione	β	$C_{19}H_{26}O_3$	200–202°	+220	+192	75.46	75.68	8.67	8.74	Aqueous methanol
	Second crop		159–163°	+117	−120		75.58		8.77	Skellysolve B + acetone
Cortisone	α of adrenosterone									
Desoxycorticosterone	β	$C_{21}H_{30}O_4$	135–140°	+204	+119°	72.80	72.81	8.73	8.61	Aqueous methanol
11α-Hydroxyprogesterone	β	$C_{21}H_{30}O_4$	156–159°	+178°	+35°	72.80	72.72	8.73	8.70	Aqueous methanol
	Second crop		118–130°	+152	−56°		72.90		8.69	Skellysolve B
Progesterone	α[b]	$C_{21}H_{30}O_3$	175–177.5°	+14.5°	−580°	76.32	75.88	9.15	9.36	Skellysolve B
	β		133–135.5°	+211°	+68°		76.06		9.33	Aqueous methanol
	Mixture			+156°	−113°		76.22		9.12	Skellysolve B
Testololactone	β	$C_{19}H_{26}O_4$	252° d.	+85°	+141°	71.67	71.56	8.23	8.44	Skellysolve B + ethanol, chloroform + methanol
	Second crop		204–240°	−52°	−295°		71.40		8.31	Acetone

[a] $\Delta M_D = M_D$ (epoxide) − M_D (conjugated ketone). The following values for the specific rotations (rounded off the nearest degree) were used: adrenosterone, +262° (ref. 12, p. 423); 4-androstene-3,17-dione, +190° (ref. 12, p. 375); desoxycorticosterone, +178° (ref. 12, p. 407); 11α-hydroxyprogesterone, +176° (ref. 14); progesterone, +200° [E. Fernholz, *Ber.*, **67**, 2027 (1934)]; testololactone, +43° [J. Fried, R. W. Thoma, and A. Klingsberg, *J. Am. Chem. Soc.*, **75**, 5764 (1953). ΔM_D for 4β,5-epoxycoprostan-3-one (ref. 6) was +198° taking $[\alpha]_D$ for 4-cholesten-3-one as +89 [A. Butenandt and A. Wolff, *Ber.*, **68**, 2091 (1935)]. In the work of Camerino, Patelli, and Vercellone (ref. 5a) the average ΔM_D for the β isomer was about +145° while for the α isomer it was about −460°. [b] See ref. 2.

cholesten-3-one is converted to the β oxide. The optical rotation which they reported for the β oxide was used as a standard in assigning the configurations given in Table I.

Cortisone (V) on treatment with alkaline hydrogen peroxide gave the epoxides of adrenosterone (VI)[7] from which the α isomer was isolated. The same compound was obtained directly from adrenosterone.



The properties of several mixtures of α and β epoxides are given in Table I. The mixture described for progesterone is the one actually employed in subsequent reactions. Based on the rotation of this material, it contained about 75% of the β epoxide and 25% of the α epoxide.

Some selected spectral data of the epoxides are given in Table II. The infrared absorption spectrum of each of the epoxides has a band between 11.56 and 11.67 μ and also a band between 12.60 and 12.68 μ. Sallmann and Tamm[8] assigned similar bands to the α,β-epoxy ketone group. A band in the 11.6 μ region has been assigned by Patterson[9] to epoxides.

The spectra (KBr disks) of the α and β epoxides of progesterone are strikingly different in the carbonyl region. The β isomer exhibits two well-defined bands (5.85 and 5.96 μ) while the α isomer displays only one band (5.84 μ, fairly broad).[10] The spectrum of the mixed epoxides ("mixture"—Table II) displays only one band even though it contains 75% of the β isomer. In chloroform solution the β isomer has a single sharp band (5.88 μ) in the carbonyl region. The spectrum of 4β,5-epoxy-11α-hydroxypregnane-3,20-dione (KBr disk) also has two carbonyl bands while the "second crop" material from the epoxidation of 11α-hydroxyprogesterone has only one.

The low-intensity ultraviolet absorption bands of the epoxy ketones are listed in Table II. Sallmann and Tamm[8] reported a bathochromic shift (from about 282 to about 300 mμ) of the six-membered cyclic ketone band on the introduction of an α,β-epoxy group. It will be seen from Table II that this shift is clearly detectable in the spectrum of the epoxide of testololactone. The spectra of the other oxides are complicated by the presence of additional keto groups.[11]

The mixture of isomeric epoxides from progesterone ([α] + 156°) on refluxing with formic acid gave 4-hydroxy progesterone (4-hydroxy-4-pregnene-3,20-dione, IV).[3] This structure was assigned on the basis of the elementary analysis, the ultraviolet absorption spectrum[12] (λ_{max} 277 mμ, log ϵ 4.06) and the infrared absorption spectrum (2.92 μ-hydroxy; 5.89 μ-C_{20} carbonyl; 6.02 and 6.16 μ-3-keto-Δ^4 system.) The molecular rotation (+585°) is consistent with that of progesterone (+628°). No evidence for the presence of any 11-hydroxylated progesterone could be found by paper chromatography of the material in the mother liquors from the formic acid reaction.

Fermentation of the mixture of isomeric epoxides from progesterone by *Rhizopus nigricans* led to the isolation of an isomerically pure hydroxylated derivative. Reduction of this fermentation product with chromous chloride[2] gave 11α-hydroxyprogesterone while treatment with hot formic acid gave a crude product having a strong absorption peak at 275 mμ. On the basis of these reactions and the molecular rotation, the fermentation product must be 4β,5-epoxy-11α-hydroxypregnan-3-one (II). The structure of this compound was confirmed by comparison with a sample of the oxide prepared by the epoxidation of 11α-hydroxyprogesterone (III).

(7) Camerino, Patelli and Vercellone (ref. 5a) indicated that they were able to isolate the epoxides of cortisone.

(8) F. Sallmann and Ch. Tamm, *Helv. Chim. Acta*, **39**, 1340 (1956).

(9) W. A. Patterson, *Anal. Chem.*, **26**, 823 (1954).

(10) It is of interest that S. Bernstein, M. Heller, and S. M. Stolar [*J. Am. Chem. Soc.*, **76**, 5675 (1954)] reported that in a Nujol mull 16α-hydroxyprogesterone displays three carbonyl bands while in chloroform it shows only the expected two bands.

(11) L. Dorfman, *Chem. Revs.*, **53**, 47 (1953).

(12) L. F. Fieser and M. Fieser, *Natural Products Related to Phenanthrene*, 3rd ed., Reinhold Publishing Corp., New York, N. Y., 1949, pp. 194–5.

TABLE II

SPECTRAL DATA OF THE 4,5-EPOXY-3-OXO STEROIDS

Epoxide Prepared from	Isomer	Infrared (KBr) λ_{max} (μ)				UV[a] λ_{max} (mμ)	E_{max}
Adrenosterone	α	5.77	5.85	11.65	12.68	295–298	120
	second crop	5.76	5.83	11.61	12.62		
4-Androstene-3,17-dione	β	5.73	5.83	11.58	12.63	295–298	90
	second crop	5.76	5.82	11.56	12.65		
Desoxycorticosterone	β	5.85	5.90[b]	11.57	12.62	285	80
11α-Hydroxyprogesterone	β	5.89	5.97	11.56	12.62	288–290	90
	second crop	5.91		11.58	12.60		
Progesterone	α	5.84		11.58	12.65	288–290	80
	β	5.85	5.96	11.62	12.65	286–290	110
		5.88[c]		11.60[c]			
	mixture	5.87		11.61	12.66		
Testololactone	β	5.81		11.58	12.67	298–302	40
	second crop	5.81		11.67	12.68		

[a] Determined in methanol at a concentration of about 0.4 g./l. [b] Shoulder. [c] Chloroform solution; stopped at 12.2 μ.

EXPERIMENTAL

Except where noted, rotations were determined using 0.5–1.0% chloroform solutions, infrared absorption spectra were obtained using pressed potassium bromide disks, and ultraviolet absorption spectra were run on methanol solutions. All melting points were taken on a Fisher-Johns block and are corrected.

The analytical determinations were made by the Analytical Department under Dr. Robert T. Dillon. The paper chromatography was performed by Miss Jeanette D. Mier.

4,5-Epoxides from 3-keto-Δ^4 steroids.[6] To a stirred solution of the steroid (0.015 mole) in methanol (200 ml.) were added dropwise and simultaneously 4*N* sodium hydroxide (24.4 ml.) and 30% hydrogen peroxide (24.4 ml.). The mixture was maintained at 20° during the addition. A white precipitate formed soon after the addition was begun. The resulting mixture was stored overnight at 2°. After dilution with water the mixture was extracted with benzene. The benzene solution was washed with water and then dried over anhydrous sodium sulfate. The residue remaining after distillation of the benzene was purified by recrystallization. The analytical data and physical constants of the oxides are summarized in Table I. Some selected spectral data are given in Table II.

The yields of the mixed epoxides (one recrystallization) ranged from 20 to 60%. The purification of the individual isomers required three or four recrystallizations.

4-Hydroxyprogesterone (IV).[8] A solution of I (4.86 g., $[\alpha]_D$ +156°) in formic acid (75 ml.) was refluxed for 45 min. The mixture was poured while hot into hot water (200 ml.). After the solution had cooled, the precipitate was collected and washed with water. Recrystallization from aqueous methanol gave crude 4-hydroxyprogesterone (2.41 g., m.p. 203–221°). A second recrystallization gave platelets melting at 221–227° (subl.).

A sample for analysis was obtained by sublimation (0.07 mm. pressure); m.p. 226–228° (presoftened; subl.); $[\alpha]_D$ +177° (chloroform); +185° (1% in ethanol); λ_{max}: 277 mμ (log ϵ = 4.06); 2.92, 5.89, 6.02 and 6.16 μ.

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.49, 76.69; H, 9.58, 9.47.

Paper chromatography failed to reveal any 11α- or 11β-hydroxyprogesterone in the mother liquors. Using a cyclohexane-phenyl Cellosolve system 4-hydroxyprogesterone migrates at approximately the same rate as progesterone.[13] (In 3 days the center of the spot of 4-hydroxyprogesterone moved approximately 9.4 cm. compared with 9.3 cm. for progesterone.)

(13) L. F. Fieser and R. Stevenson [*J. Am. Chem. Soc.*, **76**, 1728 (1954)] reported that 4-hydroxy-4-cholesten-3-one was eluted with surprising ease from acid-washed alumina.

4β,5-Epoxy-11α-hydroxypregna-3,20-dione (*II*) *by fermentation of I.* A liquid culture medium containing a commercial enzymatic digest of whey protein, corn steep liquor and dextrose was adjusted to *p*H 4.5 with concentrated hydrochloric acid and dispensed in 400 ml. quantities in 2-l. Erlenmeyer flasks. These were plugged with nonabsorbent cotton and sterilized in an autoclave for 5 min. at 120°. After cooling to room temperature, each of 20 flasks was inoculated with 3 ml. of a suspension of spores of *Rhizopus nigricans* (ATCC 6227b) prepared from a 12-day culture of the organism on a hominy grit sporulation medium. These cultures were incubated at 25° on a rotary shaker for 24 hr., at which time each received 100 mg. of 4,5-epoxypregnane-3,20-dione (I-$[\alpha]_D$ +156) in 5 ml. of ethanol. Incubation was continued for an additional 24-hr. period. The cultures were then pooled and mycelium was separated by filtration and washed with methylene chloride.

The filtrate was extracted twice with a total of 9.6 l. of methylene chloride and the solvent fractions were pooled and concentrated under reduced pressure to a volume of about 750 ml. The concentrate was extracted once with 100 ml. of 2% sodium bicarbonate and once with 100 ml. of distilled water. The solvent was removed over a steam bath under reduced pressure. The residue (2.82 g.) was chromatographed over silica (200 g.). Elution was begun with benzene and followed with an ethyl acetate–benzene mixture. The material eluted with 25% ethyl acetate was recrystallized once from aqueous methanol; yield: 690 mg.; m.p. 156–159°; $[\alpha]_D$ +184° (1% in ethanol).

Anal. Calcd. for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.88, 72.80; H, 9.04, 8.93.

This compound was identical (melting point, infrared and ultraviolet absorption spectra, no depression of the melting point on mixing) with 4β,5-epoxy-11α-hydroxypregnane-3,17-dione.

A sample of the oxide (40 mg.) was refluxed in formic acid (9 ml.) for 30 min. The formic acid was removed under reduced pressure. The ultraviolet absorption spectrum of the residue had a peak at 275 mμ (2.16 mg. %; optical density of 0.22).

11-Oxoprogesterone from II. A mixture of chromic chloride hexahydrate[2] (1.0 g.), 95% ethanol (12 ml.), and zinc dust (0.8 g.) was stirred for 2 hr. under carbon dioxide. The initial exothermic reaction was controlled by cooling the reaction vessel in an ice bath. The mixture was allowed to stand overnight under a slow stream of carbon dioxide. A solution of II (200 mg.) in ethanol (15 ml.) was added all at once with mixing. The color of the mixture turned from blue to green within several minutes. The reaction mixture was stirred for 30 min. and was then diluted with water. The diluted mixture was extracted with chloroform. The chloroform solution was washed with water and then dried over

sodium sulfate. Removal of the solvent under reduced pressure gave a residue which crystallized on cooling. Two recrystallizations from aqueous methanol gave colorless material (180 mg.) melting at 159–160.5°; [α] + 170°; λ_{max} 241 mμ (log ε = 4.20) (reported[14]: m.p. 166–168°; $[\alpha]_D$ +175.9°). The melting point of a sample mixed with authentic 11α-hydroxyprogesterone was 161–169°. The infrared absorption spectrum (KBr disk) of this compound was significantly different from that of 11α-hydroxyprogesterone which had been recrystallized from aqueous acetone.

The chromous chloride reduction product was oxidized with chromic anhydride in pyridine[15] to give 11-oxoprogesterone, m.p. 173.5–177.0; $[\alpha]_D$ +238° (acetone); reported[16]: m.p. 172–174°; $[\alpha]_D$ +238.5 ± 8° (acetone).

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(14) D. H. Peterson, H. C. Murray, S. H. Eppstein, L. M. Reineke, A. Weintraub, P. D. Meister, and H. M. Leigh, *J. Am. Chem. Soc.*, **74**, 5933 (1952).

(15) G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *J. Am. Chem. Soc.*, **75**, 422 (1953).

(16) T. Reichstein and H. G. Fuchs, *Helv. Chim. Acta*, **23**, 684 (1940).

[CONTRIBUTION FROM THE GUY AND BERTHA IRELAND RESEARCH LABORATORY, DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF NORTH DAKOTA SCHOOL OF MEDICINE]

Standard Method for Synthesis of Some 1-C^{14}-Labeled Amino Acids[1]

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A standard, 5-step method for the synthesis of 1-C^{14}-labeled glycine, DL-alanine, and DL-leucine has been investigated. The procedure may be of practical value for the preparation of carboxyl-labeled amino acids. The technique is limited to amino acids which form phthaloyl derivatives.

It has been reported that 1-C^{14}-labeled fatty acids can be prepared by decarboxylating the silver salt of the acid with a halogen to the corresponding alkylhalide, and subsequently reversing the process with $C^{14}O_2$ in the Grignard reaction.[3]

We felt that the carboxyl-labeled amino acids could be prepared in an analogous fashion; however, the silver salts of the α-amino acids when decarboxylated with a halogen produce the corresponding alkylidenimine hydrohalides rather than the α-aminoalkylhalides.[4] It was thought that the alkylidenimine compounds may have arisen through dehydrohalogenation of the α-amino alkylhalides. Blocking of the amino group would preclude this dehydrohalogenation, and might thus permit the synthesis of 1-C^{14}-labeled amino acids *via* nitrilation with NaC^{14}N and subsequent hydrolysis. This supposition was substantiated using phthalic anhydride as the blocking agent for the amino group.

Three amino acids have been prepared according to the procedure outlined in relatively good yield. These are 1-C^{14}-labeled glycine, DL-alanine, and DL-leucine.

EXPERIMENTAL

The experimental technique is identical in the case of all three amino acids, and the synthesis of glycine-1-C^{14} will be presented as an example of the method.

Phthaloylglycine. The phthaloyl derivatives of the amino acids were prepared according to the suggestion of Billman and Harting[5] A mixture of finely ground glycine[6] and a 10% excess of phthalic anhydride were fused on an oil bath for 15 min. at 185°. The liquid product, which solidified when cooled, was recrystallized twice from 10% ethanol.

Silver phthaloylglycinate. Five g. of finely powdered phthaloylglycine was suspended in 100 ml. of 10% ethanol and the pH adjusted to 6.5 with 6*N* NaOH. A 25% excess of aqueous silver nitrate was slowly added to the solution with stirring. The white precipitate, silver phthaloylglycinate, was allowed to stand in the dark for 1 hr. It was then filtered under suction. The silver salt was washed three times with water and then twice with acetone-free absolute methanol. Yield: 80–85%.

N-bromomethylphthalimide. The success of the decarboxylation demands that all glassware and reagents be scrupulously dry. The moist silver salt was placed in an oven at 65°. until hard and then powdered. Five g. of the salt was added to a flask fitted with a ground glass joint. The flask was then placed into a borosilicate glass vacuum desiccator containing P_2O_5. The desiccator was evacuated to a pressure of 1 mm. and placed in an oven at 65°. The temperature was slowly increased to 90° over a 2 hr. period. The desiccator was re-evacuated every 4 hr. Drying was continued for a total of 72 hr.

One hundred ml. of anhydrous CCl_4 (distilled and then dried over P_2O_5 for 3 days) was added to the silver phthaloylglycinate and the suspension heated to the boiling point of the solvent on a hot plate. The mixture was allowed to cool for 1 min. at room temperature, and 1.5 equivalents of dry Br_2 (shaken twice with concentrated H_2SO_4) in 5 ml. of anhydrous CCl_4, were added rapidly with shaking. The vigorous evolution of CO_2 was observed immediately. The suspension was shaken for an additional 5 min. and then refluxed gently for 1 hr. The solvent was removed at room

(1) A preliminary report of this investigation has been published.[2] The study was supported in part by a grant from the North Dakota Cancer Society.

(2) Fromm, *Federation Proc.*, **15**, 424 (1956).

(3) Howton, Davis, and Nevenzel, *J. Am. Chem. Soc.*, **76**, 4970 (1954).

(4) Hunsdiecker, Hunsdiecker, and Vogt, U. S. Patent 2,175,181 (1939).

(5) Billman and Harting, *J. Am. Chem. Soc.*, **70**, 1473 (1948).

(6) A DL mixture of alanine and leucine was employed in the synthesis of their phthaloyl derivatives.