4a,9,10,10a-octahydrophenanthrene-1,2-dicarboxylic acid (IX) which crystallized from ethyl acetate in colorless prisms, m. p. 211–213° dec.

Anal.[m] Calcd. for $C_{18}H_{22}O_5$: C, 68.0; H, 7.0. Found: C, 68.0; H, 7.1.

Summary

Two structurally isomeric adducts are formed in the reaction of citraconic anhydride with 1-vinyl-6 methoxy-3,4-dihydronaphthalene. One is a derivative of 1-methylhexahydrophenanthrene; the other has the methyl group in the 2-position of the hexahydrophenanthrene nucleus. From one a compound was synthesized whose analysis agreed with that of the methyl ether of an isomer of estrone. Preliminary studies have been carried out on the conversion of the other isomeric Diels–Alder adduct to estrone.

ANN ARBOR, MICHIGAN RECEIVED DECEMBER 1, 1947

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF INDIANA UNIVERSITY AND YALE UNIVERSITY]

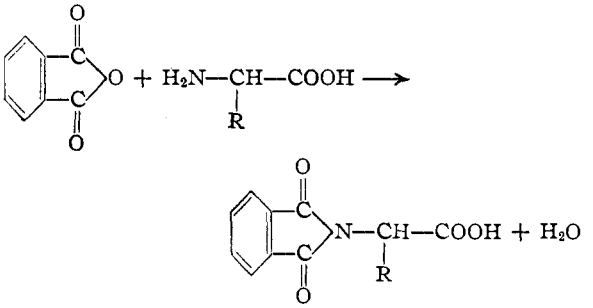
Amino Acids. V.[1] Phthalyl Derivatives

BY JOHN H. BILLMAN[2] AND WILLIAM F. HARTING[3]

Interest in amino acids has increased enormously during recent years mainly because of the many new uses which have been found for these compounds in the nutritional and medicinal fields. Additional reagents for the characterization of amino acids are accordingly useful.

Succinic anhydride and maleic anhydride were investigated as reagents but proved to be unsatisfactory. However phthalic anhydride gives compounds of excellent properties with a large number of amino acids.

Table I contains a list of the phthalyl derivative prepared in these laboratories. Phthalic anhydride condenses with amino acids according to the following general equation, the reaction being complete in fifteen minutes at 180–185°.



The recorded yields are those obtained from 0.2 to 0.5 g. of the amino acid. Much smaller amounts of the amino acid can be used with equal success. Large amounts, such as 5 g. of several of the amino acids were tried and in most cases the yields were considerably higher than those reported in the table. All of the derivatives were easily and

TABLE I

PHTHALYL DERIVATIVES OF AMINO ACIDS

Amino acid used	M. p. of derivative °C. (uncor.)	Yield, %	Analyses, % Calcd.	Found	Neutral equivalents Calcd.	Found
Glycine[a]	191–192	90	C 58.54	58.57	205	205
			H 3.41	3.56		
DL-Alanine[b]	160–161	92	N 6.39	6.45	219	218
DL-α-Amino-*n*-butyric acid[c]	95.5–96.5	65			233	231
DL-α-Amino-isobutyric acid[d]	152–153	79			233	231
DL-α-Amino-*n*-valeric acid	103–104	53	N 5.66	5.84	247	244
DL-Valine	101.5–102	54	N 5.66	5.82	247	249
DL-α-Amino-α-methylbutyric acid[e]	139–140	53	C 63.16	62.97	247	248
			H 5.26	5.44		
DL-Norleucine	111.5–112.5	38	N 5.36	5.25	261	259
DL-Leucine[f]	140–141	41			261	260
L-Leucine[5,6,g]	115–116	70	N 5.36	5.22	261	264
DL-Isoleucine	120–121	66	N 5.36	5.34	261	264
L-Glutamic acid	188–189	45	N 5.05	4.93	277	275
DL-α-Aminophenylacetic acid[h]	167–168	64	C 68.3	68.5	281	280
			H 3.9	4.0		
DL-Phenylalanine	174–175	79	N 4.74	4.81	295	300
DL-Threonine	102–103	30	N 5.62	5.81	243	246

[a] Reese, *Ann.*, **242**, 1 (1887). [b] Gabriel, *Ber.*, **38**, 634 (1905). [c] Hildesheimer, *Ber.*, **43**, 279 (1910). [d] Gabriel, *Ber.*, **44**, 59 (1911). [e] Freytog and Gabriel, *Ber.*, **48**, 648 (1915). [f] Ulrich, *Ber.*, **37**, 1695 (1904). [g] Fling, Minard and Fox report the m. p. of 118–119°. [h] McKenzie and Barrow, *J. Chem. Soc.*, **103**, 1332 (1913) (m. p. 170.5–171.5°).

(1) Paper IV, Billman and Parker, THIS JOURNAL, **67**, 1069 (1945).
(2) On leave at Yale University, September, 1946–June, 1947.
(3) Present address: Coca-Cola Company, Linton, Indiana.

quickly prepared and melted in a convenient temperature range.

Since the basic function of the amino group is suppressed by this reaction, the derivatives behave as ordinary carboxylic acids. The neutral equivalent of the derivative can therefore be used as a criterion of identity. This is particularly useful when the melting points of two derivatives are separated by only a few degrees.

A solution of phthalyl L-leucine when examined polarimetrically was found to be optically active. This confirms the findings of Fox[4] and Reese.[5] Phthalyl L-glutamic acid likewise was found to be optically active. Since racemization does not appear to occur during their preparation, phthalyl derivatives should be valuable for the rapid characterization of optically active amino acids.

Tryptophan, tyrosine, serine and taurine did not give the desired derivatives.

Preparation of Phthalyl Derivatives of Amino Acids.—In a Pyrex test-tube is placed a mixture of 0.5 g. of an amino acid and 1.0 g. of phthalic anhydride. The tube is then placed in an oil-bath, which has previously been heated to 180–185°, for fifteen minutes. During the first ten minutes, the mixture is stirred occasionally and the phthalic anhydride which sublimes and deposits on the walls of the tube is pushed down into the reaction mixture by means of a glass rod. The mixture is left undisturbed during the remaining five minutes. At the end of fifteen minutes, the test-tube is carefully removed and cooled until the liquid mass solidifies. It is then inverted and the excess phthalic anhydride sublimed on the walls is scraped out. The residue is recrystallized from 10% ethyl alcohol or water. Most of the phthalyl amino acids are very soluble in dilute alcohol. When alcohol is used, some of the derivatives oil out if too concentrated a solution of the derivative is made or if the solution is cooled too rapidly.

When working with a specific amino acid it is desirable to use an approximately one to one molar ratio of amino acid to phthalic anhydride.

(4) Fling, Minard and Fox, THIS JOURNAL, **69**, 2468 (1947).
(5) Reese, *Ann.*, **242**, 9 (1887).

Summary

A series of phthalyl derivatives of amino acids has been prepared by a general procedure and it has been shown that phthalic anhydride is a useful reagent for the identification of most of the simple amino acids.

BLOOMINGTON, IND.
NEW HAVEN, CONN. RECEIVED NOVEMBER 20, 1947

[CONTRIBUTION FROM KEDZIE CHEMICAL LABORATORY, MICHIGAN STATE COLLEGE]

Condensation of Some Tertiary Octyl Alcohols with Phenol

BY RALPH C. HUSTON, WILLIAM K. LANGDON[1a] AND LOUIS J. SNYDER[1b]

In previous communications from this Laboratory,[2] the condensations of eleven tertiary alcohols with phenol have been described. The present paper reports the condensation of the five tertiary alcohols shown in Table I.

These alcohols were prepared as described by Huston and co-workers[3] and condensed with phenol in the presence of anhydrous aluminum chloride. The yields of the *p-t*-octylphenols varied from 36 to 80%. No isomers or disubstituted products were isolated. In addition to the benzoyl esters and α-naphthylurethans of these *p-t*-octylphenols, the phenylurethans of three of them were prepared.

The position of the alkyl group in each phenol was proven by oxidation of the corresponding nitro-octylbenzene,[4] by heating in a Carius tube with 6 *N* nitric acid at 130°, to yield only *p*-nitrobenzoic acid. The corresponding *t*-octylbenzene[3] was also converted into the phenol by nitration, reduction to the amine, diazotization and hydrolysis.[2] The phenol thus synthesized was shown to be identical with the one obtained through direct condensation of the alcohol and phenol by means of melting point and mixed melting point determinations. The assignment to the alkyl group of the phenol the same structure as that of the alkyl group of the alcohol from which it is formed is based upon the following considerations:

(a) There are theoretically possible seventeen *p-t*-octylyhenols.

(b) In the rearrangement of alkyl groups during processes of condensation, primary groups may change to secondary or tertiary, secondary may change to tertiary, and tertiary may change to tertiary. Instances of the formation of appreciable yields of isomeric primary or secondary groups from tertiary groups are not known.[2b]

(c) Fifteen different *p-t*-octylphenols, corresponding to the fifteen tertiary octyl alcohols, other than 2,3,3-trimethyl-2-pentanol and 2,2,3-trimethyl-3-pentanol, have been described[2,5] or are described in this article.

When 2,3,3-trimethyl-2-pentanol is condensed with phenol, *two* *p-t*-octylphenols are formed, neither of which is identical with any of the other fifteen. The condensation of 2,2,3-trimethyl-3-pentanol with phenol gives the same two *p-t*-octyl-

(1) Present location: (a) Wyandotte Chemical Corp., Wyandotte, Mich.; (b) Ethyl Corp., Baton Rouge, La.
(2) (a) Houston and Guile, THIS JOURNAL, **61**, 69 (1939); (b) Huston and Meloy, *ibid.*, **64**, 2655 (1942).
(3) Huston, Goerner, *et al.*, *ibid.*, **70**, 1090 (1948).
(4) Malherbe, *Ber.*, **52**, 319 (1919).
(5) Huston and Krantz, *J. Org. Chem.*, **13**, 63 (1948).