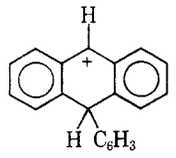
molecular ions. If 2 correctly represents the structure of the $(M - 2)^{2+}$ ion of triptycene, a similarly intense ion at the same m/e value (126) should be observed for 9,10-dideuteriotriptycene. If, however, as is the case with the singly charged ions, the hydrogens lost are those originally bonded to the aromatic ring, a shift to m/e 127 should be observed. Since the latter possibility is the case, it is concluded that structure 2 is not correct.

TABLE II
MASS SPECTRA OF TRIPTYCENE AND 9,10-DIDEUTERIOTRIPTYCENE. DOUBLY CHARGED IONS[a]

	Triptycene		9,10-Dideuteriotriptycene[b]	
	m/e	Rel intensity[c]	m/e	Rel intensity[c]
$(M)^{2+}$	127	9.3	128	7.6
$(M - 1)^{2+}$	126.5	14.7	127.5	11.1
$(M - 2)^{2+}$	126	32.4	127	27.0
$(M - 3)^{2+}$	125.5	5.8	126.5	13.5
$(M - 4)^{2+}$	125	15.1	126	9.2
$(M - 5)^{2+}$	124.5	2.8	125.5	7.0

[a] Hitachi Perkin-Elmer RMU-6D Mass Spectrometer. [b] Contains 85% d_2, 14% d_1, and 1% d_0 (see Experimental Section). [c] Relative to the $(M - 1)^+$ peak.

Since polycyclic aromatic hydrocarbons tend to exhibit molecular ions of unusually large abundance, for the $(M - 1)^+$ ion of triptycene to be of approximately equal intensity to the molecular ion suggests it to possess unusual stability. Structure **3**, which would arise by cleavage of a carbon–carbon bond to the bridgehead carbon atom and scission of the aromatic ring with loss of a hydrogen atom, is suggested for this



3a, $C_6H_3 = HC{\equiv}C{-}CH{=}CH{-}C{\equiv}C{-}$
b, $C_6H_3 = HC{\equiv}C{-}C(\mid){=}CH{-}C{\equiv}CH$

ion.[5] This is consistent with open-chain formulations for aromatic ions which have been suggested by a number of recent mass spectral studies.[6]

Experimental Section

Melting points are corrected. Infrared spectra were determined on a Perkin-Elmer Model 621 spectrophotometer. Deuterium analyses were performed by J. Nemeth, Urbana, Ill.

9,10-Dideuteriotriptycene.—Solutions of anthranilic acid (3.80 g, 27.7 mmol) and *n*-butyl nitrite (3.09 g, 30.0 mmol), each in 45 ml of butanone, were simultaneously added over a 2-hr period to a stirred refluxing solution of 9,10-dideuterioanthracene[7] (0.997 g, 5.53 mmol). The reaction mixture was refluxed for an additional 1 hr and evaporated to dryness. The residue was mixed with 50 ml of xylene and 1.71 g (17.4 mmol) of maleic anhydride, and the resulting mixture was refluxed for 1 hr and evaporated to dryness. Sodium hydroxide solution (5%, 100 ml) was added, and the mixture was heated at 100° for 1.5 hr. Extraction with chloroform and evaporation of the dried chloroform solution yielded an orange solid. Chromatography on alumina (200 g, Woelm, acidic), using benzene as the eluent, gave a white solid which was recrystallized from hexane–benzene to give the product (0.44 g, 31%): mp 251–252°; ν^{KBr} 2209 cm^{-1}; deuterium analyses gave the atom fraction deuterium as 0.1296 and 0.1300 (calcd 0.1429) in duplicate runs; low voltage mass spectrometry at 11.5 eV indicated the composition 85% d_2, 14% d_1, and 1% d_0.

Registry No.—Triptycene, 477-75-8; 9,10-dideuteriotriptycene, 17375-18-7.

Acknowledgment.—The author thanks Dr. Y. Itagaki of Jeolco, Inc., for mass spectral measurements and Mr. L. Loew for infrared measurements.

(5) The two structures shown for the C_6H_3 chain are those which would arise directly from the molecular ion. Rearrangement processes would increase the number of possibilities.

(6) For a discussion and leading references, see H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967, Chapter 1.

(7) D. E. Van Sickle and J. O. Rodin, *J. Amer. Chem. Soc.*, **86**, 3091 (1964).

The Use of (−)-Menthyl Chloroformate in the Optical Analysis of Asymmetric Amino and Hydroxyl Compounds by Gas Chromatography

JOHN W. WESTLEY AND B. HALPERN

Department of Genetics, Stanford University School of Medicine, Palo Alto, California 94304

Received June 7, 1968

The determination of optical purity of asymmetric alcohols by gas–liquid partition chromatography (glpc) of diastereoisomeric esters has been described by several investigators.[1-4] Application of these methods requires that the alcohol be quantitatively convertible into a pair of diastereoisomeric esters, so that only asymmetric alcohols which are stable during acid-catalyzed esterification conditions can be examined. We now describe the use of the reagent (−)-menthyl chloroformate (I)[5] for the optical glpc analysis of some acid-labile alcohols and α-hydroxy acids. Here diastereoisomeric carbonates, separable by glpc, can be formed in weakly basic medium at room temperature, and heat- and acid-labile compounds can be quantitatively derivatized. The reagent I is readily prepared from the commercially available (−)-menthol and phosgene; and a toluene solution of I can be kept without any noticeable deterioration over several months. The diastereoisomeric carbonates derived from α-phenylalkylcarbinols (Table I) and the common α-hydroxy fatty acid esters (Table II) have been completely resolved on packed columns, thus making this procedure suitable for quantitative optical analysis. The reagent I also reacts with amino compounds such as α-amino acid esters to form diastereoisomeric urethans separable by glpc (Table II). Since α-hydroxy and α-amino acids can be derivatized under the same reactions conditions and the diastereoisomers can be resolved on the same glpc column (Table II), we suggest the use of (−)-menthyl chloroformate for the optical analysis of depsipeptide hydrolysates. Finally some asymmetric amines such as α-phenylethylamine and α-(1-naphthyl)ethylamine have also been resolved,

(1) R. Charles, G. Fischer, and E. Gil-Av, *Israel J. Chem.*, **1**, 234 (1963); *J. Chromatog.* **17**, 408 (1965).

(2) G. E. Pollock, V. I. Oyama, and R. D. Johnson, *J. Gas Chromatog.*, **3**, 174 (1965).

(3) S. V. Vitt, M. B. Saporovskaya, I. P. Gudkova, and V. M. Belikov, *Tetrahedron Lett.*, 2575 (1965).

(4) B. Halpern and J. W. Westley, *Aust. J. Chem.*, **19**, 1533 (1966).

(5) L. A. Carpino, *Chem. Commun.*, 858 (1966).

TABLE I

GAS CHROMATOGRAPHIC SEPARATION OF ASYMMETRIC α-PHENYLALKYLCARBINOLS AS THEIR (R)-(−)-MENTHYLOXYCARBONYL DERIVATIVES[a,b]

Alcohol	Separation temp, °C	Retention time of diastereoisomers, min[c] (R)-(−), (S)-(−)	(R)-(−), (S)-(+)	(R)-(−), (R)-(+) / (R)-(−), (S)-(−)
α-Phenylmethylcarbinol	170	5.3	5.9	1.11
α-Phenylethylcarbinol	170	5.5	6.2	1.13
α-Phenylpropylcarbinol	170	6.8	7.6	1.12
α-Phenylbutylcarbinol	170	8.0	8.9	1.11
α-(p-Tolyl)propylcarbinol	170	8.1	9.3	1.15
α-Phenylcyclohexylcarbinol	200	6.45	7.0	1.09

[a] Glpc analyses were carried out on a 5 ft × 1/8 in. (3% EGS on Aeropack 30) column with a nitrogen flow of 30 ml/min. [b] All volatile compounds were characterized by mass spectrometry using a Varian 600D gas chromatograph coupled to a Finnigan 1015 quadrupole mass spectrometer. [c] (−)-Menthol has the R configuration at 1. The absolute configuration of all (−)-phenylalkylcarbinols has been shown to be S [V. Prelog and H. Scherrer, *Helv. Chim. Acta*, **42**, 2227 (1959)].

TABLE II

GAS CHROMATOGRAPHIC SEPARATION OF α-HYDROXY AND α-AMINO ACID METHYL ESTERS AS THEIR (R)-(−)-METHYLOXYCARBONYL DIASTEREOISOMERIC DERIVATIVES

Acid	Separation temp, °C	Retention time of diastereoisomers, min (R)-(−), (S)-(−)	(R)-(−), (R)-(+)	(R)-(−), (R)-(+) / (R)-(−), (S)-(−)
Lactic	170	3.85	4.2	1.09
α-Hydroxyisovaleric	170	5.0	3.7	1.14
α-Hydroxyisocaproic	170	6.8	7.8	1.15
3-Phenyllactic	200	8.5	9.7	1.14
Alanine	170	6.6	7.0	1.06
Valine	170	9.05	10.0	1.10
Leucine	170	11.9	12.75	1.07
Phenylalanine	200	13.1	14.4	1.10

[a] Glpc analyses were carried out on 5 ft × 1/8 in. column packed with 5% QF-1 on Aeropak 30. The nitrogen flow during analyses was 30 ml/min.

but the degree of resolution of the diastereoisomeric urethans (α = 1.06) is less than for the previously described TFA-L-prolylamides (α = 1.22).[6]

Experimental Section

Preparation of (−)-Menthyl Chloroformate.—1-Menthol (15.63 g, 0.1 mol) and quinoline (12.9 g, 0.1 mol) were added to a solution of phosgene (20 g, 0.2 *M*) in toluene (100 ml) at 0°, and the mixture was stirred overnight. The quinoline hydrochloride was filtered off, and the excess phosgene was removed by bubbling nitrogen through the filtrate. The solution was then transferred to a 100-ml standard flask containing calcium carbonate and stored at 0°. Under these conditions, the solution, which contains 1 mmol of the reagent/ml, can be kept for several months without any noticeable decomposition.

The use of pyridine instead of quinoline in the preparation of the reagent, as described by Carpino,[5] leads to the formation of significant amounts of di-(−)-menthyl carbonate[7] {mp 106–107°; $[\alpha]_D$ −87.3° (*c* 1.18, EtOH). *Anal.* Calcd for $C_{21}H_{38}O_3$: C, 74.52; H, 11.32. Found: C, 74.81; H, 11.46}.

Steric Analysis of Asymmetric α-Phenylalkylcarbinols.—Racemic α-phenylmethylcarbinol (122 mg, 1 mmol) and pyridine (0.1 ml) were added to the standard solution of (−)-menthyl chloroformate in toluene (1.1 ml, 1.1 mmol), and the reaction mixture was allowed to stand at room temperature for 30 min. After washing with water and drying with sodium sulfate, a part of the solution (~3 μl) was injected into the gas chromatograph. Glpc retention time assignment (Table I) for the diastereoisomers were made on the basis of the glpc analysis of optically pure (−)-menthyloxycarbonyl-(−)-α-phenylmethylcarbinol {mp 71.2°; $[\alpha]_D$ −113° (*c* 1, EtOH). *Anal.* Calcd for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 75.22; H, 9.40} prepared from (−)-α-phenylmethylcarbinol[8] and the O-(−)-menthyloxycarbonyl derivatives obtained from (+)-α-phenylbutylcarbinol[8] and (+)-α-phenylcyclohexylcarbinol.[9]

(6) B. Halpern and J. W. Westley, *Chem. Commun.*, 34 (1966).
(7) E. Salomae, *Ann. Acad. Sci. Fennicae*, **94**, 1 (1959).
(8) P. A. Levene and L. A. Mikeska, *J. Biol. Chem.*, **70**, 355 (1926).
(9) P. A. Levene and L. A. Mikeska, *ibid.*, **75**, 587 (1927).

Steric Analysis of α-Hydroxy and α-Amino Acids.—The α-hydroxy or -amino acid (1 mmol) was treated with methanolic hydrogen chloride (5 ml, 1.25 *N*), and after 3 hr at room temperature, the solvent was removed under vacuum. An excess of the reagent solution (1.1 ml, 1.1 mmol) and pyridine (0.2 ml) was then added and the reaction left for 30 min at room temperature. After washing and drying, a sample (3 μl) was injected into the gas chromatograph (Table II). Glpc retention time assignments for the disastereoisomers were made on the basis of the analysis of optically pure (−)-menthyloxycarbonyl-L-(−)-3-phenyllactic acid methyl ester {mp 66°; $[\alpha]_D$ −62° (*c* 1, EtOH). *Anal.* Calcd for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34. Found: C, 69.51; H, 8.53}, racemic (−)-methyloxycarbonyl-DL-phenylalanine methyl ester {mp 65–69°; $[\alpha]_D$ −66.6° (*c* 1, EtOH). *Anal.* Calcd for $C_{21}H_{31}NO_4$: C, 69.77; H, 8.65; N, 3.88. Found: C, 69.78; H, 8.72; N, 3.93}, optically pure (−)-methoxycarbonyl-L-phenylalanine methyl ester {mp 79°; $[\alpha]_D$ −61.1° (*c* 1, EtOH). Found: N, 3.56}, (−)-methyloxycarbonyl-D-phenylalanine methyl ester {mp 68–70°; $[\alpha]_D$ −67° (*c* 1, EtOH). Found: N, 3.50}, and the (−)-methyloxycarbonyl derivatives obtained from commercially available (+)-lactic acid, (−)-α-hydroxyisocaproic acid, and the L-amino acids.

Steric Analysis of Amines.—Derivatization of amines was done as described for the alcohols. The urethans were chromatographed on a 5 ft × 1/8 in. (5% QF1 on Aeropack 30) column using a nitrogen flow of 30 ml/min. The retention times for the diastereoisomers from racemic α-phenylethylamine were 9.5 min for the (*R*)-(−), (*R*)-(−) and 10.1 min for the (*R*)-(−),-(*R*)-(+) at a column temperature of 180°, and for the diastereoisomers from α-(1-naphthyl)ethylamine the times were 6.6 min for the (*R*)-(−), (*S*)-(−) and 7.0 min for the(*R*)-(−), (*R*)-(+) compounds at a column temperature of 230°. The glpc retention time assignment were made on the basis of the analysis of the optically pure compounds: N-(−)-methylocarbonyl-(−)-α-phenylethylamine {mp 112–113°; $[\alpha]_D$ −107° (C, 1% EtOH). *Anal.* Calcd for $C_{19}H_{29}NO_2$: C, 75.20; H, 0.63; N, 4.62. Found: C, 75.35; H, 9.67; N, 4.79}, N-(−)-methyloxycarbonyl.(+)-α-phenylethylamine {mp 114°; $[\alpha]_D$ −2.7° (*c* 1.15, EtOH)-Found: C, 75.21; H, 9.60; N, 4.76}, N-(−)-methyloxycarbonyl-(+)-α-(1-naphthyl)ethylamine {mp 135°; $[\alpha]_D$ −60.8° (*c* 1.07, EtOH). *Anal.* Calcd for $C_{23}H_{31}NO_2$: C, 78.14; H,

8.84; N, 3.96. Found: C, 78.15; H, 8.76; N, 4.23}, and N-(−)-menthyloxycarbonyl-(−)-α-(1-naphthyl)ethylamine {mp 119°; $[\alpha]_D$ −43.1° (*c* 1.18, EtOH). Found: C, 78.28; H, 8.67; N, 4.17}.

Registry No.—(−)-Methyl chloroformate, 14602-86-9; (−)-menthyloxycarbonol-(−)-α-phenylmethylcarbinol, 17397-39-6; (−)-menthyloxycarbonyl-L-(−)-3-phenylacetic acid methyl ester, 17397-40-9; racemic (−)-menthyloxycarbonyl-DL-phenylalanine methyl ester, 17397-47-6; (−)-menthyloxycarbonyl-L-phenylalanine methyl ester, 17397-41-0; (−)-menthyloxycarbonyl-D-phenylalanine methyl ester, 17397-42-1; N-(−)-menthyloxycarbonyl-(−)-α-phenylethylamine, 17397-43-2; N-(−)-menthyloxycarbonyl-(+)-α-phenylethylamine, 17397-44-3; N-(−)menthyloxycarbonyl-(+)-α-(1-naphthyl)ethylamine, 17397-45-4; N-(−)-menthyloxycarbonyl-(−)-α-(1-naphthyl)ethylamine, 17397-46-5; α-phenylmethylcarbinol, 98-85-1; α-phenylethylcarbinol, 93-54-9; α-phenylpropylcarbinol, 614-14-2; α-phenylbutylcarbinol, 583-03-9; α-(*p*-tolyl)-propylcarbinol, 6282-37-7; α-phenylcyclohexylcarbinol, 945-49-3; tactic acid methyl ester, 17392-83-5; α-hydroxyisovaleric acid methyl ester, 17417-00-4; α-hydroxyisoenproic acid methyl ester, 17392-84-6; 3-phenylacetic acid methyl ester, 17417-01-5; alanine methyl ester, 10065-72-2; valine methyl ester, 4070-48-8; leucine methyl ester, 2666-93-5; phenylalanine methyl ester, 2577-90-4.

Acknowledgments.—This investigation was supported by National Aeronautics and Space Administration Grant NsG 81.

Cyclization of N-Oxalyl-α-amino Acid Derivatives[1]

WALTER R. HEARN AND JORGE MEDINA-CASTRO

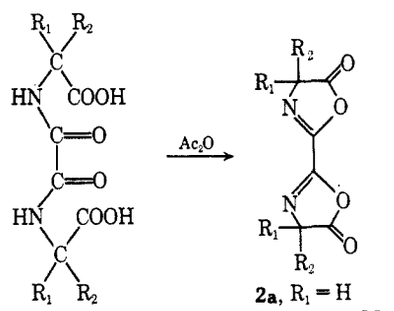
Department of Biochemistry and Biophysics, Iowa State University, Ames, Iowa 50010

Received April 29, 1968

We have reported synthesis of the cyclic L-proline-N-oxalic anhydride[2] by treatment of L-proline in an inert solvent with excess oxalyl chloride. Under the same or milder conditions, glycine, DL-valine, or L-leucine gave tarry products from which no anhydride could be isolated. After removal of excess oxalyl chloride and even after treatment with boiling water, however, the crude reaction products sometimes gave a positive hydroxamic acid test, suggesting the presence of some anhydride or other acylating species.

One possibility considered for reaction of oxalyl chloride with an α-amino acid possessing a primary amino group was N-acylation followed by an alternative cyclization to an azlactone [5(4H)-oxazolone; 2-oxazolin-5-one]. The known tendency of azlactones to polymerize under mild conditions[3] would account for the intractable tars found whenever azlactone formation was possible (*i.e.*, when NH was still present in the N-acylamino acid). In this paper we report an investigation of N-oxalyl derivatives of α-aminoisobutyric acid containing the NH requisite for azlactone formation but lacking the α-H atom requisite for polymerization *via* acylation on the 4 position of any azlactone formed.

No examples of 2-oxazolin-5-ones containing a carboxy, carbalkoxy, or carboxamide group attached to the 2 position could be found in the literature, although a large number of N-oxalyl derivatives of α-amino acids have been prepared, in particular the N,N′-oxalylbis(α-amino acids).[4] Cleaver and Pratt prepared a large number of N,N′-diacylbis(α-amino acids) and successfully dehydrated them to 5-oxazolones in hot acetic anhydride.[5] If α-H atoms were present, degradation occurred, presumably *via* the Dakin–West reaction,[6] unless cyclization conditions were carefully controlled. Even with careful control, however,[5] the N,N′-oxalylbis(α-amino acids) (**1a**) failed to dehydrate to the corresponding diazlactones (**2a**).



1a, $R_1 = H$
b, $R_1, R_2 = Me$

2a, $R_1 = H$
b, $R_1, R_2 = Me$

We have now been able to carry out such a cyclization on N,N′-oxalylbis(α-aminoisobutyric acid) (**1b**) in hot acetic anhydride to obtain a small yield of 2,2′-bis(4,4-dimethyl-5-oxazolone) (**2b**). The structure of **2b** was indicated by elemental analysis and infrared (ir) spectrum and confirmed by the nuclear magnetic resonance (nmr) spectrum, which showed only a strong singlet (CH_3) at τ 8.54; no indication of NH or OH was present in either the ir or nmr spectrum. Compound **2b** is unusually stable for a "saturated-type" azlactone[3] without aromatic substitution, in contrast to 4,4-dimethyl-5-oxazolone itself, for example.[7] In addition to the 10% yield of azlactone, a 32% yield was obtained of a compound presumed by analysis and behavior to be a mixed anhydride of 1 mol each of the starting material and acetic acid. Mild hydrolysis of either compound regenerated **1b**.

A compound of perhaps greater interest was N-oxalyl-α-aminoisobutyric acid (**3**), since cyclization could lead either to the anhydride **4** (as in the proline case) or to 4,4-dimethyl-5-oxazolone-2-carboxylic acid (**5**). Acylation of α-aminoisobutyric acid ethyl ester by ethoxalyl chloride went smoothly, but difficulties

(1) Journal Paper No. J-5856 of the Iowa Agriculture and Home Economics Experiment Station, Ames, Iowa, Project No. 1384. Abstracted from the M.S. thesis of J. Medina-Castro, Iowa State University, Ames, Iowa, 1963. J. Medina-Castro's address: Departamento de Química Orgánica, Facultad de Química, Bioquímica y Farmacia, Universidad de Chile, Santiago, Chile.

(2) W. R. Hearn and R. E. Worthington, *J. Org. Chem.*, **32**, 4072 (1967).

(3) H. E. Carter, *Org. Reactions*, **3**, 198 (1946).

(4) J. T. Bornwater, *Rec. Trav. Chim.*, **31**, 105 (1912). For other references, see W. R. Hearn and R. A. Hendry, *J. Amer. Chem. Soc.*, **79**, 5212 (1957).

(5) C. S. Cleaver and B. C. Pratt, *ibid.*, **77**, 1544 (1955).

(6) H. D. Dakin and R. West, *J. Biol. Chem.*, **78**, 745 (1928).

(7) M. T. Leplawy, D. S. Jones, G. W. Kenner, and R. C. Sheppard, *Tetrahedron*, **11**, 39 (1960).