15 hr. On cooling to room temperature the precipitate was collected and washed with three 100-ml. portions of hot methanol. The solid was then boiled with 500 ml. of methanol and filtered hot. Yield: 32 g. or 91%. M.p. 241–242°. Recrystallization from 6 l. of glacial acetic acid gave 31 g. of a product which had a melting point of 242°, in agreement with the literature value.

**1-Anthraquinonesulfenyl Chloride.**—To 21.75 g. of 1-anthraquinonyl benzyl sulfide in 800 ml. of dry benzene was added 8.9 g. of sulfuryl chloride. The mixture was warmed and shaken until a reaction occurred and a clear solution resulted. After filtering, the solution was allowed to cool to room temperature. The resulting crystalline precipitate was collected and the mother liquor was concentrated to obtain a second and a third crop. Yield: 17.9 g. or 99%. M.p. 220–223° (first crop), m.p. 216–220° (later crops) (lit. m.p. 224°). Recrystallization did not improve the melting point of the lower melting product.

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## Symmetrical Anhydrides of Hydroxy Acids[1]

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The symmetrical anhydrides of carboxylic acids containing unprotected hydroxyl functions apparently have not been prepared or described. This paper reports the synthesis and characterization of a series of these derivatives and establishes the symmetrical anhydrides of hydroxy acids as a known class of compounds.

In the course of amide syntheses using mixed carboxylic–carbonic anhydrides of the hydroxy fatty acids obtainable from castor oil,[2a,b] a series of experiments was performed to determine the reactivity of the secondary alcohol functions under the reaction conditions employed. The hydroxyl groups in these compounds were found to be unreactive at 0° toward ethyl chloroformate or toward the mixed carboxylic–carbonic anhydrides[3] formed from ethyl chloroformate and the triethylammonium salts of the carboxylic acids. Neither carbethoxylation nor esterification could be discounted *a priori* since both types of reaction are known to take place with secondary alcohols[4,5] under conditions suitable for the mixed anhydride reaction.

Since the alcohol functions in question were quite inert it seemed worth while to determine if the mixed anhydride method could be utilized for symmetrical anhydride formation with these hydroxy acids, as has been done in a few cases involving other carboxylic acids,[6,7] and if the products could be isolated despite the presence of both hydroxyl and anhydride functions in the same molecule.

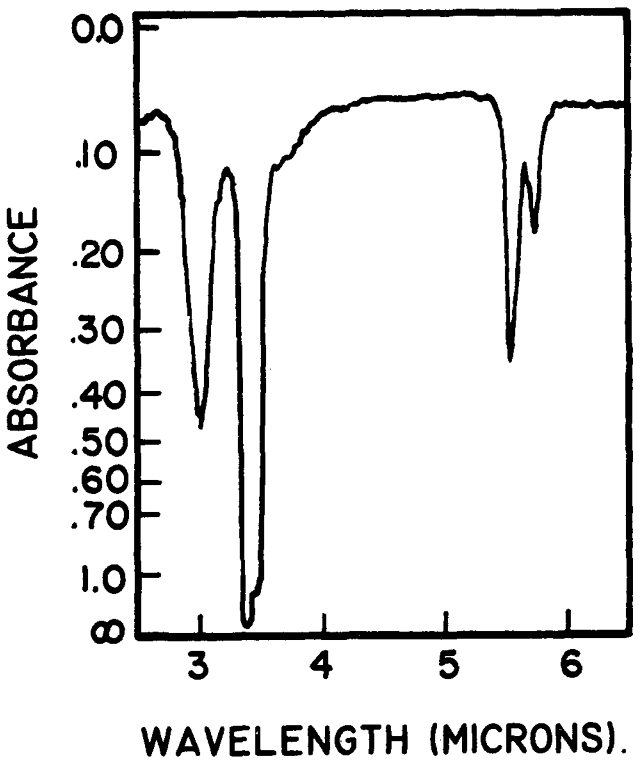
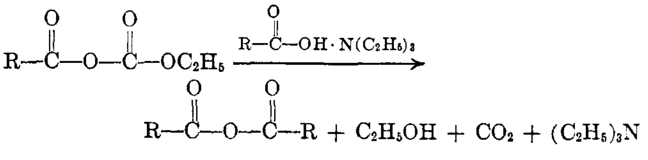


Fig. 1.—Infrared spectrum of 9,10-dihydroxyoctadecanoic anhydride: Nujol mull.

Reaction of the mixed carboxylic–carbonic anhydride of each hydroxy acid with one equivalent of the carboxylate anion of the same acid (present as the triethylammonium salt) in tetrahydrofuran at 0° gave a series of crystalline compounds, the symmetrical anhydrides, with melting points about 20° higher than those of the parent acids. These products (listed in Table I with yields and other pertinent data) have the expected infrared spectra for symmetrical hydroxy acid anhydrides. A typical example (Fig. 1) shows the hydroxyl band at 3.0 $\mu$, and the paired carbonyl bands characteristic of carboxylic acid anhydrides.[8]

Though it has not been widely employed, this method of anhydride synthesis is a convenient, high yield procedure. Attack of the carboxylic acid anion on the carboxyl carbonyl of the mixed anhydride appears to be



$$R-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-OC_2H_5 \xrightarrow{R-\overset{O}{\overset{\|}{C}}-OH\cdot N(C_2H_5)_3} R-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-R + C_2H_5OH + CO_2 + (C_2H_5)_3N$$

rapid and straightforward. No detectable side reactions occurred in the cases reported here, and the yields were 95% or greater.

The hydroxy acid anhydrides are slowly decomposed at temperatures considerably above their melting points to give acidic material and polymeric esters. At ordinary temperatures, they apparently can be stored indefinitely. The 12-hydroxy-*cis*-9-octadecenoic symmetrical anhydride is best kept below 0°, but the other

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[1] Presented before the American Chemical Society Meeting in Miniature, Berkeley, Calif., December 17, 1962.

[2] (a) 12-Hydroxy-*cis*-9-octadecenoic, 12-hydroxy-*trans*-9-octadecenoic, 12-hydroxyoctadecanoic, 9,10-dihydroxyoctadecanoic, and 9,10,12-trihydroxyoctadecanoic acids; (b) T. H. Applewhite, Jane S. Nelson, and L. A. Goldblatt, *J. Am. Oil Chemists' Soc.*, **40**, 101 (1963).

[3] J. R. Vaughan, Jr., *J. Am. Chem. Soc.*, **73**, 3547 (1951); R. A. Boissonnas, *Helv. Chim. Acta*, **34**, 874 (1951); T. Wieland and H. Bernhard, *Ann. Chem.*, **572**, 190 (1951).

[4] N. F. Albertson, *Org. Reactions*, **12**, 157 (1962), has suggested such reactions as a possible cause of difficulties in mixed anhydride syntheses using hydroxy amino acids.

[5] L. F. Fieser, "Experiments in Organic Chemistry," 3rd Ed., D. C. Heath and Co., Boston, Mass., 1955, p. 318, describes the carbethoxylation of alcohols with ethyl chloroformate.

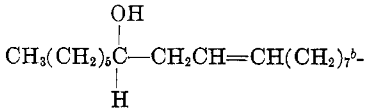
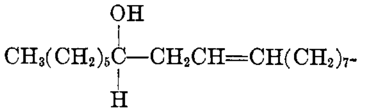
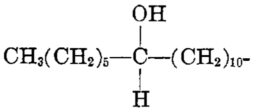
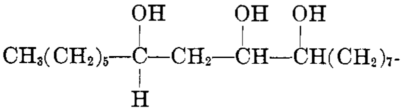
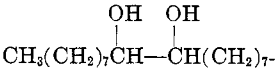
[6] L. N. Akimova and N. I. Gavrilov, *Zh. Obshch. Khim.*, **23**, 417 (1953); *Chem. Abstr.*, **48**, 3904 (1954).

[7] E. Schipper and J. Nichols, *J. Am. Chem. Soc.* **80**, 5714 (1958).

[8] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., Methuen and Co. Ltd., London, 1958, p. 127.

TABLE I

HYDROXY ACID ANHYDRIDES

| $(R\underset{\underset{O}{\|}}{C})_2O$<br>R— | Yield,[a] % of theory | M.p., °C. | Infrared bands—Hydroxyl region, μ | Infrared bands—Carbonyl region, μ | % C Calcd. | % C Found | % H Calcd. | % H Found |
|---|---|---|---|---|---|---|---|---|
|  $CH_3(CH_2)_5\overset{OH}{\underset{H}{C}}-CH_2CH=CH(CH_2)_7{}^{b}$-<br>*cis* | 95 | 35–35.5 | 2.90[c]<br><br>2.75[d] | 5.56[c]<br>5.76[c]<br>5.50[d]<br>5.71[d] | 74.7 | 74.5 | 11.5 | 11.4 |
|  $CH_3(CH_2)_5\overset{OH}{\underset{H}{C}}-CH_2CH=CH(CH_2)_7$-<br>*trans* | 96 | 64–64.5 | 3.0[c]<br><br>2.79[d] | 5.52[c]<br>5.76[c]<br>5.51[d]<br>5.72[d] | 74.7 | 74.7 | 11.5 | 11.4 |
|  $CH_3(CH_2)_5-\overset{OH}{\underset{H}{C}}-(CH_2)_{10}$- | 99 | 88–89 | 3.0[c] | 5.52[c]<br>5.77[c] | 74.2 | 74.1 | 12.1 | 12.1 |
|  $CH_3(CH_2)_5-\overset{OH}{\underset{H}{C}}-CH_2-\overset{OH}{C}H-\overset{OH}{C}H(CH_2)_7$- | Quant. | 132–133 | 2.95[c]<br>3.02[c] | 5.52[c]<br>5.72[c] | 66.8 | 66.9 | 10.9 | 10.9 |
|  $CH_3(CH_2)_7\overset{OH}{C}H-\overset{OH}{C}H(CH_2)_7$- | Quant. | 91–92 | 3.0[c] | 5.52[c]<br>5.72[c] | 70.3 | 70.5 | 11.5 | 11.4 |

[a] Washed and dried products (*cf.* text). [b] Recrystallized prior to analysis (*cf.* text). [c] Smear or Nujol mull. [d] Carbon tetrachloride solution.

TABLE II

ANHYDRIDE DERIVATIVES

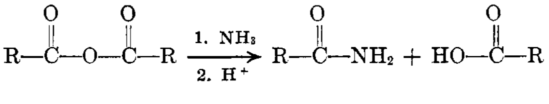
| Compound | M.p., °C. | Infrared bands[a]—Hydroxyl region, μ | Infrared bands[a]—Carbonyl region, μ | % C Calcd. | % C Found | % H Calcd. | % H Found | % N Calcd. | % N Found |
|---|---|---|---|---|---|---|---|---|---|
| 9,10,12-Trihydroxyoctadecanamide | 136-137 | 2.90<br>3.10 | 6.05 | 65.2 | 65.4 | 11.2 | 11.2 | 4.23 | 4.16 |
| 9,10-Dihydroxyoctadecanamide | 113-113.5 | 2.96<br>3.10 | 6.08 | 68.5 | 68.4 | 11.8 | 11.7 | 4.44 | 4.45 |
| 12-Hydroxyoctadecanamide | 111-112 | 2.88<br>3.00<br>3.08 | 6.02 | 72.2 | 72.1 | 12.4 | 12.2 | 4.68 | 4.68 |
| 12-Hydroxy-*cis*-9-octadecenamide | 65.5-66.5[b,c] | 2.95<br>3.10 | 6.03<br>6.10 | 72.7 | 72.5 | 11.9 | 11.7 | 4.71 | 4.64 |
| 12-Hydroxy-*trans*-9-octadecenamide | 86.5-87.5[c,d] | 2.90<br>2.95<br>3.03 | 6.02 | 72.7 | 72.5 | 11.9 | 11.8 | 4.71 | 4.52 |
| 9,10,12-Trihydroxyoctadecanoic acid | 108[e] | 3.00 | 5.90 | 65.0 | 65.1 | 10.9 | 10.8 | ... | ... |
| 9,10-Dihydroxyoctadecanoic acid | 92.5-93.5[f] | 2.99<br>3.05 | 5.80<br>5.88 | 68.3 | 68.5 | 11.5 | 11.4 | ... | ... |
| 12-Hydroxyoctadecanoic acid | 80-80.5[g] | 3.10 | 5.90 | 72.0 | 71.9 | 12.1 | 11.9 | ... | ... |
| 12-Hydroxy-*trans*-9-octadecenoic acid | 49.5-50[h] | 3.00<br>3.07 | 5.90 | 72.5 | 72.4 | 11.4 | 11.3 | ... | ... |
| 12-Hydroxy-*cis*-9-octadecenoic acid | Oil | 2.95 | 5.85 | [i] | ... | ... | ... | ... | ... |

[a] Nujol mulls or smears. [b] M.p. 66°, J. Bouis, *Ann. chim. phys.*, [3] **44,** 77 (1855). [c] No depression on admixture with authentic sample. [d] M.p. 91–93°, T. H. Rowney, *Jahresber. Fortschr. Chem.*, 533 (1855). [e] M.p. 108–109°, J. T. Scanlan and D. Swern, *J. Am. Chem. Soc.*, **62,** 2309 (1940). Starting material used here: 106–108°. [f] M.p. 94–95°, D. Swern, J. T. Scanlan, and G. B. Dickel, *Org. Syn.*, **39,** 15 (1959). Starting material used here: 92–93°. [g] M.p. 80.5–81°, F. Straus, H. Heinze, and L. Salzmann, *Chem. Ber.*, **66,** 631 (1933). Starting material used here: 79.5–80°. [h] M.p. 50.5–51.1°, M. A. McCutchon, R. T. O'Connor, E. F. DuPre, L. A. Goldblatt, and W. G. Bickford, *J. Am. Oil Chemists' Soc.*, **36,** 115 (1959). Starting material used here: 49.8–50.9°. [i] Identical to starting acid with respect to infrared spectrum and $R_f$ on a thin-layer chromatogram.

members of this series show no detectable change after standing at room temperature for several months.

These anhydrides are also relatively inert on treatment with water, dilute acid, or dilute alkali. This is evident in that organic solutions of the anhydrides can be washed with dilute acids, bases, or water without appreciable decrease in yield or purity.

The anhydrides rapidly react to form equimolar quantities of amide and parent acid on treatment with ammonia followed by acidification. These derivatives have the correct infrared spectra, melting points, and elemental analyses (Table II).



$$R-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-R \xrightarrow[2.\ H^+]{1.\ NH_3} R-\overset{O}{\overset{\|}{C}}-NH_2 + HO-\overset{O}{\overset{\|}{C}}-R$$

Since limited experimentation with lactic acid in mixed anhydride system led to inconclusive results and intractable mixtures, no attempt was made to prepare its symmetrical anhydride. We found that mandelic acid undergoes carbethoxylation when treated with equimolar amounts of ethyl chloroformate and triethylamine in the usual mixed anhydride method. Similar results were reported earlier by Fischer and Fischer[9] when they treated mandelic acid with excess methyl chloroformate. This procedure also appears inapplicable to phenols as exemplified by the results with *p*-hydroxycinnamic acid. Attempts to prepare the amide of this acid using the mixed anhydride method led to carbethoxylation of the phenolic hydroxyl rather than to mixed anhydride formation, so again symmetrical anhydride formation was not attempted. Examination of the applications and limitations of this symmetrical anhydride-forming system with other hydroxy acids is now in progress.

### Experimental[10]

All melting points were obtained in capillary tubes in an electrically heated block and are uncorrected. Infrared spectra were obtained as Nujol mulls; a Perkin-Elmer Model 137 Infracord with sodium chloride optics was used. Mixed carboxylic–carbonic anhydrides were prepared at 0° in tetrahydrofuran, as previously described,[2b] and used without isolation.

**Symmetrical Anhydrides.**—Table I. Equimolar quantities (typical 0.01-mole scale) of hydroxy acid and freshly distilled triethylamine were dissolved in about 50 ml. of tetrahydrofuran (THF) for each 0.01 mole of acid. This solution was added from a dropping funnel to a well stirred solution of the corresponding mixed anhydride in tetrahydrofuran kept at or near 0° with an ice–salt bath. One molar equivalent of acid salt was used for each equivalent of mixed anhydride. After this addition, the system was allowed to come to room temperature, with stirring, and to stand overnight. The solution was then filtered from the triethylamine hydrochloride, which had precipitated during preparation of the mixed anhydride, and the precipitate was washed with tetrahydrofuran. The filtrate and washings were combined and the solvent removed *in vacuo* at room temperature on a rotary evaporator. The product was taken up in ether or chloroform, depending on its solubility, and washed with dilute hydrochloric acid and 1 *M* sodium carbonate solution followed with water until the washes tested neutral to pH paper. The organic solutions were dried over magnesium sulfate, filtered, and returned to the rotary evaporator for removal of solvent at room temperature. Yields were determined at this point. After this work-up, all of the compounds were essentially pure (Table I) and free of starting acid (Fig. 1); the only further treatment prior to analysis in the case of the saturated hydroxy anhydrides and 12-hydroxy-*trans*-9-octadecenoic anhydride was drying in a vacuum oven at room temperature and 0.01 mm. The 12-hydroxy-*cis*-9-octadecenoic anhydride was recrystallized from petroleum ether at −10°, then dried at room temperature and 0.01 mm.

**Anhydride Derivatives.**—Table II. Anhydrous ammonia gas was passed through a solution of hydroxy acid anhydride in tetrahydrofuran at room temperature. The tetrahydrofuran was removed on the rotary evaporator to leave an equimolar mixture of hydroxy acid ammonium salt and the corresponding amide. Weights obtained corresponded to theory. These product mixtures were dissolved in absolute methanol and separated on a column of macroreticular quaternary ammonium ion-exchange resin.[11] After recovery of the amide, a methanol solution of acetic acid was used to remove the hydroxy acid from the column. Each of the derivatives was recrystallized from 95% ethanol, the amides at room temperature and the slightly more soluble acids at 0°, and dried *in vacuo* at 40°.

**Acknowledgment.**—We thank Miss Geraldine E. Secor for performing the elemental analyses.

(9) E. Fischer and H. O. L. Fischer, *Chem. Ber.*, **47**, 768 (1914).

(10) Reference to a company or product name does not imply approval or recommendation of the product by the U. S. Department of Agriculture to the exclusion of others that may be suitable.

(11) Amberlyst XN-1001, Rohm and Haas Co., *cf.* R. Kunin, E. Meitzner, and N. Bortnick, *J. Am. Chem. Soc.*, **84**, 305 (1962).

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# Reaction of Cinnamic Acid Dibromide with Iodide Ion

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Providence, Rhode Island*

*Received February 4, 1963*

The conversion of vicinal dibromides to olefins by reaction with iodide ion has been investigated by several groups.[2-10] The reaction is usually reported to be first order in iodide ion and first order in dibromide. It has been shown that the elimination may follow a direct mechanism involving nucleophilic attack of iodide ion on bromine in a typical E2 process resulting in *trans* elimination[7] or may involve $S_N2$ replacement of bromine by iodine on carbon followed by rapid collapse of the iodobromide.[8] This process gives the appearance of *cis* elimination of the bromine atoms.[9] The E2 mechanism apparently is preferred except for 1,2-dibromo compounds where displacement of the primary bromide is facile.

In connection with other work[11] we had occasion to use the reaction of iodide ion with cinnamic acid dibromides as an analytical method. In view of the fact that third-order kinetics had been reported for this process and because the stereochemistry had not been studied, we investigated the reaction of *erythro*-2,3-dibromo-3-phenylpropionic acid, hereafter referred to as *trans*-cinnamic acid dibromide, in the solvents 80% aqueous acetic acid and 80% aqueous methanol. The reaction was followed by titrating the iodine liberated.

## Results

***trans*-Cinnamic Acid Dibromide.**—The conditions and specific rate constants obtained for the second-order reaction of *trans*-cinnamic acid dibromide with iodide ion are listed in Table I. The order of the reaction with respect to iodide ion and with respect to dibromo acid was determined by the method of initial slopes.[12] The values for the order with respect to iodide ion as determined for three different sets of reaction conditions were 0.96, 0.98, and 0.97. Similarly the order with respect to dibromo acid was found to be 1.0. The effect of ionic strength and the specific effect of bromide ion were tested by the addition of sodium perchlorate or of potassium bromide. The specific rate constants were calculated from the rate expression for a second-order reaction in the integrated form. The

(1) Colgate University, Hamilton, N. Y.

(2) A. Slator, *J. Chem. Soc.*, **85**, 1697 (1904).

(3) E. Biilmann, *Rec. trav. chim.*, **36**, 313 (1917).

(4) C. F. van Duin, *ibid.*, **43**, 341 (1924); **45**, 345 (1926); **47**, 715 (1928).

(5) R. T. Dillon, *J. Am. Chem. Soc.*, **54**, 952 (1932).

(6) T. L. Davis and R. Heggie, *J. Org. Chem.*, **2**, 470 (1937).

(7) S. Winstein, D. Pressman, and W. G. Young, *J. Am. Chem. Soc.*, **61**, 1645 (1939).

(8) J. Hine and W. H. Brader, *ibid.*, **77**, 361 (1955).

(9) W. M. Schubert, H. Steadly, and B. S. Rabinovitch, *ibid.*, **77**, 5755 (1955).

(10) W. G. Lee and S. I. Miller, *J. Phys. Chem.*, **66**, 555 (1962).

(11) E. R. Trumbull, R. T. Finn, K. M. Ibne-Rasa, and C. K. Sauers, *J. Org. Chem.*, **27**, 2339 (1962).

(12) R. Livingston in Weissberger, "Investigations of Rates and Mechanism of Reactions, Technique of Organic Chemistry," Vol. VIII, Interscience Publishers Inc., New York, N. Y., 1953, p. 182.