tion from which the product rapidly crystallized as colorless needles, wt. 5.50 g. (71.5%), m.p. 109–110°, $[\alpha]^{26}D$ −17.3 ± 0.5° (*c* 2, ethanol). The literature melting point is 111°.[12]

When the preparation was repeated using the "standard" conditions previously reported,[1] a 72% yield of recrystallized material was also obtained; m.p. 109–110°.

Ethyl L-Phenylalanylglycinate Hydrobromide.—A 7.69-g. (0.02 mole) sample of ethyl carbobenzoxy-L-phenylalanylglycinate, 300 mg. of palladium black[13] and 1.5 cc. of glacial acetic acid were placed in 150 cc. of absolute alcohol and hydrogen was bubbled through the mixture at room temperature. Carbon dioxide evolution began immediately and was complete within 1 hour. The catalyst was filtered off and the solution concentrated to about 25 cc. and acidified with a slight excess of 1 *N* alcoholic hydrogen bromide. The solution was then reconcentrated to 25 cc. by vacuum distillation and diluted with 50 cc. of ether to precipitate a small amount of "gel-like" material. This impurity was filtered off and the filtrate was diluted with an additional 200 cc. of ether to give a clear solution from which the product crystallized as colorless plates on standing, wt. 4.05 g. (61%), m.p. 135–136°; $[\alpha]^{27}D$ +40.2 ± 0.5° (*c* 2, water). Recrystallization did not change the melting point or rotation.[14]

A second crop of material was obtained from the filtrate by concentration to dryness and recrystallization of the solid residue as above, wt. 0.65 g. (10%), m.p. 131–134°.

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[12] M. Bergmann and J. S. Fruton, *J. Biol. Chem.*, **118**, 414 (1937).

[13] R. Willstätter and E. Waldschmidt-Leitz, *Ber.*, **54**, 128 (1921).

[14] Reference 10 gives m.p. 135–136° and $[\alpha]D$ +40° (*c* 2, water) for this compound.

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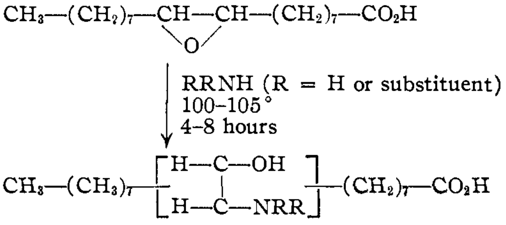
Chemistry of Epoxy Compounds. XIV.[1] Reaction of *cis*-9,10-Epoxystearic Acid with Ammonia and Amines[2]

BY DANIEL SWERN AND THOMAS W. FINDLEY

RECEIVED JULY 17, 1952

This note reports the opening of the oxirane ring of *cis*-9,10-epoxystearic acid with ammonia and amines (equation 1), the isolation of pure 9,10(10,9)-aminohydroxystearic acid and moderately pure N-substituted aminohydroxystearic acids, and potentiometric titration curves for several of these amino acids in the presence and absence of formaldehyde.



$$CH_3-(CH_2)_7-\underset{\diagdown O \diagup}{CH-CH}-(CH_2)_7-CO_2H \xrightarrow[\text{4–8 hours}]{\text{RRNH (R = H or substituent), 100–105°}} CH_3-(CH_3)_7-\left[\begin{array}{c} H-C-OH \\ | \\ H-C-NRR \end{array}\right]-(CH_2)_7-CO_2H \quad (1)$$

Experimental

Materials Used.—*cis*-9,10-Epoxystearic acid, m.p. 59.5°, was prepared from oleic acid by epoxidation with perbenzoic acid.[3] A.C.S. reagent grade concentrated aqueous ammonia was used. The Eastman Kodak Co. White Label Grades of 25% aqueous methylamine, 33% aqueous ethylamine, 33% aqueous dimethylamine and diethylamine were used without further purification. Diethylamine was diluted with approximately two parts of water to yield a 33% solution. Aniline was freshly distilled before use.

Preparation of 9,10(10,9)-Aminohydroxystearic Acid.—A typical experiment is described. Six grams (0.02 mole) of 9,10-epoxystearic acid and 14 ml. of 14.5 *N* aqueous ammonia (0.20 mole) were placed in a Pyrex glass combustion tube sealed at one end and partially constricted at the other. The tube was immersed in Dry Ice–acetone for several minutes and the constricted end of the tube was sealed off. The tube was then placed within a steel pipe which was closed with threaded caps at each end, and the whole assembly was heated and rotated in an oil-bath at 100–105° for four hours. The steel pipe was removed from the bath and allowed to cool to room temperature. The glass tube was again immersed in Dry Ice for several minutes and the tube was opened. The contents were transferred quantitatively to an evaporating dish and 205 ml. of 0.1 *N* aqueous sodium hydroxide was added. The solution was boiled until the odor of ammonia could not be detected and the vapors gave no test for alkalinity with test paper (about one to two hours were required). Sufficient (approximately 205 ml.) 0.1 *N* hydrochloric acid was then added to neutralize the sodium hydroxide and yield a mixture whose *p*H was about 6. A viscous oil precipitated which solidified on standing overnight; weight 6.1 g. The crude 9,10(10,9)-aminohydroxystearic acid was crystallized twice from 95% ethanol (8 ml./g.) at 0°, yielding 3.5 g. (55%) of pure material, m.p. 153–155°. In duplicate experiments, yields ranging from 30–62% were obtained. *Anal.* Calcd. for $C_{18}H_{37}O_3N$: C, 68.6; H, 11.8; N, 4.44; neut. equiv., 315.5. Found: C, 68.9; H, 11.7; N, 4.51; neut. equiv. (formaldehyde present), 316.

Preparation of N-Substituted 9,10(10,9)-Aminohydroxystearic Acids.—The reaction of aqueous methylamine (12.4 g.) with *cis*-9,10-epoxystearic acid (6.0 g.) for eight hours at 100–105° yielded a viscous oil which did not solidify after removal of excess methylamine and acidification, as described in the preceding section under 9,10(10,9)-aminohydroxystearic acid. The reaction product was evaporated to dryness and separated from sodium chloride by solution in 40 ml. of boiling absolute ethanol. The ethanol solution was cooled to −50° for one week, yielding 1 g. of 9(10)-N-methylamino-10(9)-hydroxystearic acid, m.p. 100–103°. *Anal.* Calcd. for $C_{19}H_{39}O_3N$: N, 4.25; neut. equiv., 329.5. Found: N, 4.59; neut. equiv. (formaldehyde present), 331.5. The filtrate was evaporated to dryness yielding 5 g. of viscous oil; N, 4.19; neut. equiv., 348. It was evident, therefore, that the reaction yielded mainly 9(10)-N-methylamino-10(9)-hydroxystearic acid.

Aqueous ethylamine (13.7 g.) and *cis*-9,10-epoxystearic acid (6.0 g.) yielded 7.3 g. of a viscous oil after separation of the sodium chloride as described above. *Anal.* Calcd. for 9(10)-N-ethylamino-10(9)-hydroxystearic acid, $C_{20}H_{41}O_3N$: N, 4.08. Found: N, 4.36. No precipitate was obtained when a solution of this product in absolute ethanol was cooled to −50°.

Aqueous dimethylamine (13.7 g.) and *cis*-9,10-epoxystearic acid (6.0 g.) yielded 7.7 g. of yellow viscous oil from the alcohol solution. *Anal.* Calcd. for 9(10)-N,N-dimethylamino-10(9)-hydroxystearic acid, $C_{20}H_{41}O_3N$: N, 4.08. Found: N, 3.67. This product showed appreciable water solubility; a 5% solution was only slightly turbid.

Aqueous diethylamine (21 g.) and *cis*-9,10-epoxystearic acid (6.0 g.) yielded 7.1 g. of a semi-solid. *Anal.* Calcd. for 9(10)-N,N-diethylamino-10(9)-hydroxystearic acid, $C_{22}H_{45}O_3N$: N, 3.77. Found: N, 2.64.

cis-9,10-Epoxystearic acid (24 g., 0.08 mole) and aniline (72 g., 0.8 mole) were heated on the steam-bath for six hours in a nitrogen atmosphere. The reaction mixture was poured into 1 liter of 1.5 *N* hydrochloric acid in a separatory funnel and the aqueous layer was discarded. The upper oil layer was washed with four 500-ml. portions of 1.5 *N* hydrochloric acid, then with 5% sodium chloride until the wash was neutral, and twice with distilled water. The upper layer was dissolved in ethyl acetate and the solution was dried over anhydrous calcium sulfate. Filtration and evaporation of solvent yielded 16–25 g. of reddish-brown oil. Analysis indicated that it contained about 80% 9(10)-N-phenylamino-10(9)-hydroxystearic acid and about 20% of the anilide of this substance. *Anal.* Calcd. for 9(10)-N-phenylamino-10(9)-hydroxystearic acid, $C_{24}H_{41}O_3N$: N, 3.57; neut. equiv., 391.5; calcd. for the anilide, $C_{30}H_{46}O_2N_2$: N, 6.0. Found: N, 4.05; neut. equiv., 475–481.

Surface Active Properties of N-Substituted 9,10(10,9)-Aminohydroxystearic Acids.—Although 9(10)-N,N-di-

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[1] For paper XIII, see THIS JOURNAL, **74**, 1655 (1952).

[2] Article not copyrighted.

[3] D. Swern, T. W. Findley and J. T. Scanlan, THIS JOURNAL, **66**, 1925 (1944).

methylamino-10(9)-hydroxystearic acid was the only compound studied which showed appreciable water solubility, 9(10)-N-methylamino- and 9(10)-N-ethylamino-10(9)-hydroxystearic acids showed slight solubility. Surface tensions of 0.2% solutions of these compounds under neutral, acidic and alkaline conditions are shown in Table I. Measurements were made with the Du Nouy Interfacial Tensiometer.

TABLE I

SURFACE TENSION OF 0.2% SOLUTIONS OF N-SUBSTITUTED 9,10(10,9)-AMINOHYDROXYSTEARIC ACIDS

Aminohydroxystearic acid	t, °C.	pH[a]	Surface tension, dynes/cm.
Dimethyl-	19	4	36
Dimethyl-	19	7	33
Dimethyl-	19	9	38
Dimethyl-	19	11	37
Methyl-	24	4	36
Methyl-	24	7	33
Methyl-	24	9	38
Methyl-	24	11	39
Methyl-[b]	24	7	34
Ethyl-	24	5	37
Ethyl-	24	7	33
Ethyl-	24	10	36

[a] The pH values other than 7 were obtained by the addition of a sufficient quantity of aqueous sodium hydroxide or hydrochloric acid. [b] Half-saturated with sodium chloride.

Potentiometric Titrations.—Approximately 0.3-0.6 g. of N-substituted or unsubstituted aminohydroxystearic acids were dissolved in 100 ml. of 70% aqueous ethanol and the titration curves were determined using a pH meter with external electrodes. With the exception of the titration of 9(10)-N-phenylamino-10(9)-hydroxystearic acid, the compounds studied showed no sharp inflection in the titration curves if formaldehyde was absent from the titration mixture. To obtain satisfactory titration curves, it was necessary to employ formaldehyde. Approximately 10 ml. of 35% aqueous formaldehyde, neutralized with dilute aqueous alkali to phenol red, was used in the solvent system. Figure 1 shows the titration curves for pure 9(10),10(9)-aminohydroxystearic acid in the absence (A) and presence (B) of formaldehyde, and the crude reaction product of *cis*-9,10-epoxystearic acid with aqueous ammonia prior to recrystallization (C, formaldehyde present). Figure 2 shows the titration curves for 9(10)-N-methylamino-10(9)-hydroxystearic acid in the absence (A) and presence (B) of formaldehyde and Fig. 3, curves A and B, show similar data for 9(10)-N-phenylamino-10(9)-hydroxystearic acid.

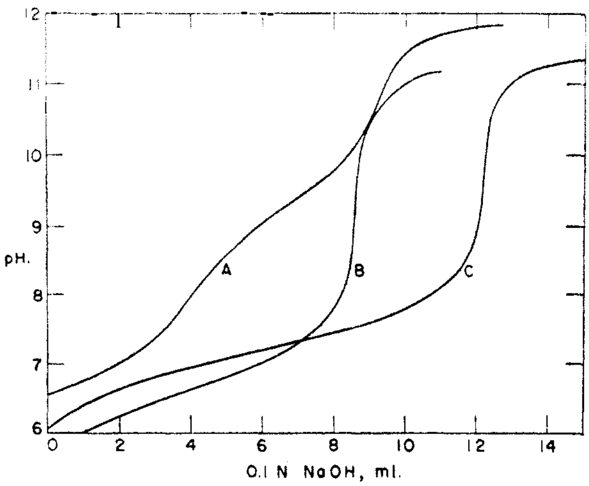

Fig. 1.—Titration curves for 9,10(10,9)-aminohydroxystearic acid: A, 0.3270 g. of pure sample, formaldehyde absent; B, 0.2720 g. of pure sample, formaldehyde present; neut. equiv., 316 (8.61 ml. of 0.1 N NaOH required); C, 0.4162 g. of crude reaction product, formaldehyde present; neut. equiv., 340 (12.24 ml. of 0.1 N NaOH required).

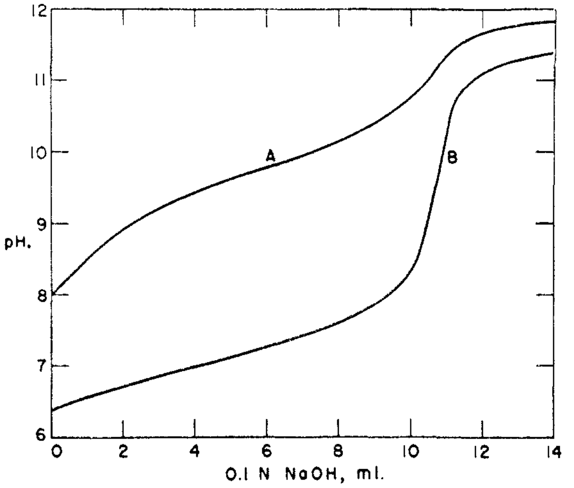

Fig. 2.—Titration curves for 9(10)-N-methylamino-10(9)-hydroxystearic acid: A, 0.3722 g. of sample, formaldehyde absent; B, 0.3563 g. of sample, formaldehyde present; neut. equiv., 330 (10.80 ml. of 0.1 N NaOH required).

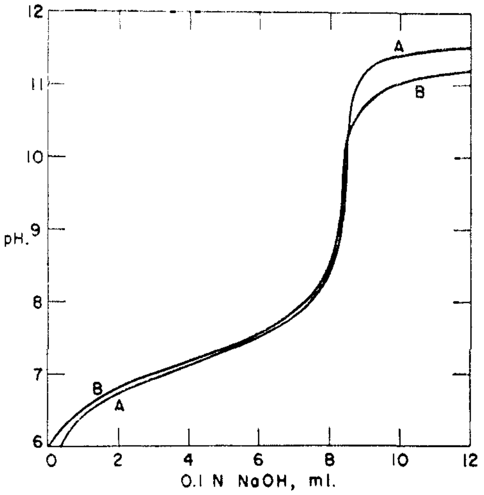

Fig. 3.—Titration curves for 9(10)-N-phenylamino-10(9)-hydroxystearic acid: A, 0.4014 g. of sample, formaldehyde absent; neut. equiv., 475 (8.45 ml. of 0.1 N NaOH required); B, 0.4024 g. of sample, formaldehyde present; neut. equiv., 481 (8.37 ml. of 0.1 N NaOH required).

Discussion

With the exception of 9(10)-N-phenylamino-10-(9)-hydroxystearic acid, the titration curves in the absence of formaldehyde show that substituted and unsubstituted aminohydroxystearic acids behave as typical amino acids, namely, they exist in solution as salts even in 70% ethanol. Formaldehyde, since it suppresses the basic properties of the nitrogen, permits a typical titration curve to be obtained. The failure of 9(10)-N-phenylamino-10(9)-hydroxystearic acid to show any difference in behavior in the absence or presence of formaldehyde is attributed to the lower basic strength of nitrogen containing a phenyl substituent, thereby preventing salt formation from occurring.

The relatively high water-solubility of 9(10)-N, N-dimethylamino-10(9)-hydroxystearic acid is attributed to the higher basic strength of the dimethylamino moiety, which would enhance salt formation and, consequently, solubility in water. The surface-active properties of the compounds are to be expected in view of their salt formation and structural relationship to amine salts of long-chain fatty acids in which properly balanced hydrophilic and hydrophobic groups are present. Sinking time measurements on canvas disks immersed in aqueous solutions of these substances show that the canvas is penetrated rapidly but not nearly so rapidly as in aqueous solutions of the sodium salt of dioctyl sulfosuccinate of the same concentration.

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Further Aspects of the Schmidt Reaction

BY ROGER D. WESTLAND AND WILLIAM E. MCEWEN

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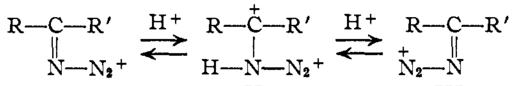
The Schmidt reaction of *p*-methylbenzophenone has been studied both by Smith and Horwitz[1] and Sherk, *et al.*[2] Smith and Horwitz, using trichloroacetic acid as the solvent and only a relatively small amount of sulfuric acid as the catalyst, obtained benz-*p*-toluidide and *p*-toluanilide in a ratio of 54:46. Sherk, *et al.*, by passing hydrogen azide slowly through a mixture of the ketone in an excess of sulfuric acid, with benzene as the solvent, obtained benz-*p*-toluidide in a yield of 82%. The divergent results suggested that product ratios might be very sensitive to the experimental conditions in this reaction.

Inasmuch as the Schmidt reaction of aldehydes gives rise to different product ratios as the sulfuric acid concentration is altered,[3] it seemed reasonable to suppose that the same might hold true for the Schmidt reaction of ketones. Specifically, it was thought that the geometrically isomeric cations, I and III, first proposed by Smith[4] as product controlling intermediates (*trans* rearrangement) in the Schmidt reaction of ketones, might undergo an acid-catalyzed interconversion, possibly *via* the conjugate acid, II. As Smith and Horwitz[1] have suggested, it is possible for "migration aptitudes"[5] to influence the product ratio, if the rate of interconversion of the *syn* and *anti* forms of the intermediate compares in magnitude with the rate of migration of either R (phenyl) or R′ (*p*-tolyl). In this connection, it has been established[6,7] that in the Schmidt reaction of 1-phenyl-1-*p*-tolylethylene, the *p*-tolyl group migrates about five times as fast as the phenyl group.



I II III

The Schmidt reaction of *p*-methylbenzophenone has been repeated under two different sets of conditions in order to determine any possible change in product ratio with increase in the sulfuric acid concentration. By use of an 8:1 molar ratio of sulfuric acid to the ketone, there was obtained a product ratio of 51% benz-*p*-toluidide to 49% *p*-toluanilide. The conditions of Sherk, *et al.*,[2] were employed in a second run. Here also there was obtained a ratio of benz-*p*-toluidide to *p*-toluanilide of 53:47. Since our method of analysis (see the experimental section) is probably accurate to not more than ± 5%, these results are in agreement with that of Smith and Horwitz,[1] who used a different method of analysis of the products.

Since the *p*-anisyl group migrates at a faster rate than the *p*-tolyl group in the Schmidt reaction of 1,1-diarylethylenes,[6,7] and since the methoxyl group is a stronger base strengthening substituent than the methyl group, both effects should enhance the possibility of a change in product ratio with change in sulfuric acid concentration in the Schmidt reaction of *p*-methoxybenzophenone. Even in this case, however, in the presence of a large excess of sulfuric acid, there was obtained a ratio of benz-*p*-anisidide to anisanilide of 66:34, in substantial agreement with the ratio of 61:39 reported by Smith and Horwitz.[1,8] Hence we conclude that a change in sulfuric acid concentration does not affect product ratios in the Schmidt reaction of *p*-substituted benzophenones.

Prior to the publication of Boyer's[9] work on conjugate addition reactions of hydrazoic acid, we had investigated the Schmidt reaction of 2-vinylpyridine. The rearrangement usually exhibited by arylethylenes was not detected, and only 1-α-pyridyl-2-azidoethane was isolated, the product obtained by Boyer in the absence of sulfuric acid.

Experimental[10]

Azeotropic Esterification of a Known Mixture of *p*-Toluic Acid and Benzoic Acid.—To a solution of 6.80 g. (0.05 mole) of *p*-toluic acid and 6.10 g. (0.05 mole) of benzoic acid in 75 cc. of absolute ethanol and 75 cc. of benzene was added 1 cc. of concentrated sulfuric acid. The mixture was slowly distilled through an 18″ electrically heated Vigreux column, to which an azeotropic head was attached. When the temperature of the overhead vapor reached 72°, the distillation was stopped and the remaining alcohol and benzene removed *in vacuo*.

A small amount of water was added to the residual mixture, which was then neutralized with powdered sodium carbonate. The mixture was extracted with ether, dried over anhydrous sodium sulfate, filtered and the ether evaporated. Distillation of the residue through a Todd column

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[1] P. A. S. Smith and J. P. Horwitz, THIS JOURNAL, **72**, 3718 (1950).

[2] J. K. Sanford, F. T. Blair, J. Arroya and K. W. Sherk, *ibid.*, **67**, 1941 (1945).

[3] W. E. McEwen, W. E. Conrad and C. A. VanderWerf, *ibid.*, **74**, 1168 (1952).

[4] P. A. S. Smith, *ibid.*, **70**, 320 (1948).

[5] There is growing evidence that the term "migratory aptitude" has little meaning. A superior interpretation is based on the concept of a driving force due to the participation of the migrating group in the attainment of the transition state. See S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber and J. Corse, *ibid.*, **74**, 1113 (1952), and other recent papers by Winstein, *et al.*, for the elaboration of this theory.

[6] W. E. McEwen, M. Gilliland and B. I. Sparr, *ibid.*, **72**, 3212 (1950).

[7] W. E. McEwen and N. B. Mehta, *ibid.*, **74**, 526 (1952).

[8] *Cf.* P. A. S. Smith and B. Ashby, *ibid.*, **72**, 2503 (1950).

[9] J. H. Boyer, *ibid.*, **73**, 5284 (1951).

[10] Analyses by Oakwold Laboratories, Alexandria, Va. All m.ps. are corrected.