

9,10-epoxystearamide only. To a well-stirred solution of 18.3 g. (0.05 mole) of *N*-(*n*-hexyl)-oleamide⁶ (iodine number, 69.3; m. p. 31.0–31.5°) in 10 ml. of glacial acetic acid at 20°, 55 ml. of approximately 1 *M* peracetic acid solution³ (0.06 mole) was added within five minutes. The reaction temperature was maintained between 20 and 25° by external cooling, and a peroxide oxygen analysis was run at hourly intervals.⁷ After about four hours, 85–90% of the calculated quantity of peracetic acid had been consumed, and the reaction mixture was then poured into about 500 ml. of ice-water. A granular solid precipitated, which was filtered off and washed with several portions of cold water. After being air-dried, the crude *N*-(*n*-hexyl)-9,10-epoxystearamide (purity, about 84%), m. p. 62–63.5°, weighed 18.6 g. Recrystallization to constant melting point from acetone at 25° resulted in a 53% yield of pure *N*-(*n*-hexyl)-9,10-epoxystearamide, m. p. 66.0–66.5°.

The quantity of glacial acetic acid required to dissolve 0.05 mole of the unsaturated amide varied with the amide employed, and was just sufficient to give a homogeneous solution at 20–25°. *N*-(*n*-Decyl)-oleamide required 840 ml. of glacial acetic acid. *N*-(*n*-Dodecyl)-oleamide was

(7) Wheeler, *Oil and Soap*, **9**, 89 (1932).

too insoluble in acetic acid at 20–25°; it was dissolved in 200 ml. of acetic acid at 30°, and the epoxidation reaction was conducted at that temperature. Higher temperatures should be avoided because of the increased rate of decomposition of peracetic acid and also because of the increased rate at which the oxirane ring is opened by acetic acid.

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Summary

Peracetic acid in acetic acid solution has been used to epoxidize some long-chain mono-unsaturated amides. 9,10-Epoxystearamide and a series of *N*-substituted 9,10-epoxystearamides have been prepared in 30–90% yield by the epoxidation of oleamide and *N*-substituted oleamides.

PHILADELPHIA 18, PA.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

Synthesis of 5-(1-Methoxypropyl)-5-alkyl (or 5-Phenyl) Hydantoin¹

BY HENRY R. HENZE, GEORGE L. SUTHERLAND AND GEORGE W. BENZ

Recently, the synthesis has been reported² of a series of 5-alkyl (or 5-phenyl)-5-propoxymethyl-hydantoin which have been shown elsewhere³ to possess considerable activity as anticonvulsants. In particular, the propoxymethyl and isopropoxymethyl derivatives were found to be worthy of intensive study, which, in turn, led to clinical testing of the latter.

Because of the desirable pharmacological activity exhibited by members of this series, it appeared to be desirable to prepare some related hydantoin, and especially the isomeric compound, 5-(1-methoxypropyl)-5-phenylhydantoin. The hydantoin, fifteen in number, were prepared from the corresponding alkyl (or phenyl) 1-methoxypropyl ketones⁴ by means of the Bucherer procedure.⁵

Experimental

The Bucherer procedure,⁵ in some instances with slight modification, was used to convert the ketones into the corresponding hydantoin. In general, the reactants were mixed in the proportions of one equivalent of ketone, 1.2–1.5 equivalent of sodium or potassium cyanide, and 3–5 equivalents of U. S. P. ammonium carbonate. The cyanide was dissolved in the minimal amount of water, and the solution was added to a solution of the ketone in five times its volume of ethyl alcohol. Water or alcohol were added, if needed, to produce a homogeneous solution in about 70% alcohol. After addition of the ammonium carbonate, the mixture was warmed at about 60° for from

six to fifteen hours. In the case of the ketones containing either a 1-methylethyl, 1-methylbutyl, or 2-methylbutyl group, it was necessary to heat the reaction mixture in a pressure vessel at 100° for twelve hours.

The reaction mixtures were acidified with concentrated hydrochloric acid and chilled; solid material formed and was separated by filtration. Concentration of the mother liquors yielded additional products. In some cases, adequate purification was attained through repeated recrystallization from diluted alcohol. In other instances, it proved beneficial to dissolve the crude hydantoin in 10% sodium hydroxide solution and to reprecipitate the hydantoin by saturating the alkaline solution with carbon dioxide. Fifty per cent. alcohol-water, benzene, or benzene-dioxane served best for final recrystallization.

The phenyl hydantoin, after recrystallization from alcohol-water, and from benzene-dioxane, was dried for twenty-four hours at room temperature in a vacuum (about 30 inches) produced by an oil pump. The mass of white needles melted at 210–212°; analysis indicated mono-hydration of the hydantoin.

Anal. Calcd. for $C_{13}H_{18}N_2O_3$: C, 62.88; H, 6.50; N, 11.28; Calcd. for $C_{13}H_{18}N_2O_3 \cdot H_2O$: C, 58.63; H, 6.81; N, 10.52. Found: C, 58.65; 58.73; H, 7.06, 7.13; N, 10.71, 10.65.

Although drying this material for twenty-four hours in a vacuum oven (30 inches) at 100° did not result in any change in the melting point, a loss of weight was observed.

Anal. Calcd. for $C_{13}H_{16}N_2O_3 \cdot H_2O$: H_2O , 6.76. Found: H_2O , 6.98.

The results of analyses of this anhydrous phenylhydantoin derivative, together with similar data for the other fourteen derivatives, may be found in Table I.

Through the courtesy of Parke, Davis and Co., five members of this series of 5-alkyl-5-(1-methoxypropyl)-hydantoin (namely, the ethyl, *s*-butyl, amyl, isoamyl and cyclohexyl) have been subjected to testing for activity as anticonvulsants. Although a slight degree of activity was found, the group appears to be markedly less active than is the alkoxyethyl series.

(1) From the M.A. thesis of G. W. Benz, August, 1946, of G. and L. Sutherland, August, 1947.

(2) Henze, Melton and Forman, *THIS JOURNAL*, **70**, 2438 (1948).

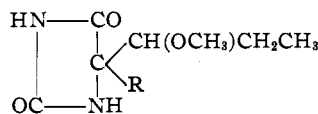
(3) Merritt, Putnam and Bywater, *J. Pharmacol.*, **84**, 67 (1945).

(4) Henze, Benz and Sutherland, *THIS JOURNAL*, **71**, 2122 (1949).

(5) Bucherer and Lieb, *J. prakt. Chem.*, [2] **141**, 5 (1934).

TABLE I

-R	M. p., °C.	Yield, %	Carbon, %		Hydrogen, %		Nitrogen, %	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
CH ₃	234-235 (dec.)	44	51.60	51.59	7.58	7.80	15.05	15.08
C ₂ H ₅	216.0-216.5	90	53.98	53.99	8.05	8.33	13.99	14.12
C ₃ H ₇	188-189	52	56.05	56.09	8.47	8.55	13.08	13.33
CH(CH ₃) ₂	206-208	66	56.05	56.13	8.47	8.53	13.08	13.08
C ₄ H ₉	197-198	48	57.86	58.07	8.83	8.95	12.27	12.39
CH(CH ₃)C ₂ H ₅	221-222	28	57.86	57.86	8.83	8.98	12.27	12.39
CH ₂ CH(CH ₃) ₂	241-242	36	57.86	57.99	8.83	8.73	12.27	12.06
C ₅ H ₁₁	171.0-171.5	74	59.50	59.64	9.15	9.47	11.56	11.63
CH(CH ₃)C ₃ H ₇	154-155	62	59.50	59.98	9.15	9.29	11.56	11.46
CH ₂ CH(CH ₃)C ₂ H ₅	221-222	12	59.50	59.75	9.15	8.97	11.56	11.74
CH ₂ CH ₂ CH(CH ₃) ₂	216-218	87	59.50	59.58	9.15	9.35	11.56	11.44
CH(C ₂ H ₅) ₂	213.0-213.5	33	59.50	59.58	9.15	9.41	11.56	11.69
C ₆ H ₁₃	147-148	87	60.91	60.85	9.44	9.65	10.93	11.17
Cyclo-C ₆ H ₁₁	243-245	32	61.39	61.57	8.72	8.85	11.03	11.19
C ₆ H ₅	210-212	92	62.88	62.82	6.50	6.76	11.28	11.39



Summary

Thirteen 5-alkyl-5-(1-methoxypropyl) hydantoin, and the analogous 5-cyclohexyl and 5-

phenyl derivatives have been prepared from the corresponding ketones.

AUSTIN, TEXAS

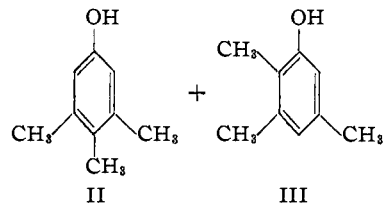
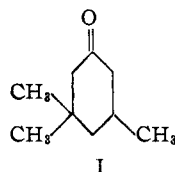
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[CONTRIBUTION FROM CHANDLER LABORATORY, COLUMBIA UNIVERSITY]

Sulfonic Acids in the Rearrangement and Aromatization of Some Cyclic Ketones¹

BY W. VON E. DOERING AND F. MARSHALL BERINGER²

Unexpectedly, the reaction of dihydroisophorone (3,3,5-trimethylcyclohexanone, I) with 30% oleum³ for one week followed by steam distillation produces small amounts of 3,4,5-trimethylphenol^{4,5,6} (*sym*-hemimellitenol, II) and 2,3,5-trimethylphenol^{7,8,9,10} (isopseudocumenol,



(1) This work, taken from a dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science of Columbia University, was presented in part at the 112th meeting of the American Chemical Society, September 16, 1947, New York, N. Y.

(2) Columbia University Fellow, 1945-1946; Allied Chemical and Dye Corporation Fellow, 1946-1947. Present address: Department of Chemistry, The Polytechnic Institute of Brooklyn, Brooklyn 2, N. Y.

(3) The experiment was vainly designed to realize an additional acid-catalyzed fission of β -trisubstituted ketones, as exemplified by the cleavage of camphor to carvenone [Bredt, Rochussen and Monheim, *A. Ann.*, **314**, 376 (1901)].

(4) Horning has surveyed alicyclic-aromatic conversions in *Chem. Rev.*, **33**, 89 (1943).

(5) Auwers and Saurwein, *Ber.*, **55**, 2372 (1922).

(6) Auwers and Wieners, *ibid.*, **58**, 2815 (1925).

(7) Edler, *ibid.*, **18**, 630 (1885); Smith, Hoehn and Ungnade, *J. Org. Chem.*, **4**, 351 (1939); Horning, *et al.*, *ibid.*, **9**, 552 (1944).

(8) Kruber and Schmidt, *Ber.*, **64**, 2274 (1931).

(9) Caldwell and Thompson, THIS JOURNAL, **61**, 2354 (1939); Baddeley, *J. Chem. Soc.*, 330 (1944).

(10) While our material melts (66-66.5°) much lower than that reported^{11,12} (93° to 96°), the coincidences of melting point of the dibromo derivative (147-148°; variously reported^{13,14} from 147° to 152°) and the phenylurethan (169.5-170.5°; reported,¹⁵ 174°) leave little doubt that our material is either a low-melting allotrope of III or a eutectic mixture of II and III, the latter alternative being

III). Under essentially identical conditions isophorone (3,3,5-trimethylcyclohexanone, IV) is aromatized smoothly (54% yield) and exclusively to II.¹¹ When treated with 5% oleum in acetic anhydride, IV is transformed (38%) into 3,4,5-trimethylphenyl acetate. In all reactions large amounts of sulfur dioxide are evolved.

While it is clear that IV may be an intermediate in that part of the aromatization of I which leads to II, further examination suggests the involvement of the grossly impure character of the crude phenylurethan.

(11) The absence of III removes the possibility that the III formed in the aromatization of I arises by a subsequent Jacobsen-type rearrangement of II.