Summary

The preparation of *p*-nitro- and of *p*-amino-diphenyl ether has been described; from the amino compound seven differently substituted phenoxy-ureas and thio-ureas have been prepared. These ureas which are analogs of the sweet compound dulcin (*p*-phenetyl-urea) are without a sweet taste and in the case of two of the thio-ureas the taste was found to be bitter, although not as bitter as that of other very closely related thio-ureas, thus indicating the effect of the phenoxy group in decreasing both the sweet and the bitter taste.

CLEVELAND, OHIO

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

THE PREPARATION AND USE OF ALDEHYDE ESTERS FORMED BY OZONATION OF THE METHYL ESTERS OF VARIOUS UNSATURATED ACIDS

BY C. R. NOLLER[1] WITH ROGER ADAMS

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The aldehyde esters formed by ozonation of such esters as methyl oleate, methyl undecylenate and methyl erucate should have wide application in synthetic work and should offer valuable starting materials, especially for the synthesis of acids of high molecular weight. This research had as its object the study of the experimental details by which these aldehyde esters could be readily made. Satisfactory results were obtained and no difficulty was encountered in the isolation of over 55% of the calculated amount of aldehyde ester boiling over a range of 5°. With especial care these yields could be increased. In addition, pelargonic aldehyde in yields of 60–70% was obtained from methyl oleate and methyl erucate.

Previous investigators have ozonized oleic,[2] elaidic,[2a] linoleic,[3] α- and β-linolenic,[4] ricinoleic,[3] erucic,[5] brassidic,[5] undecylenic[3b] and eleostearic[6] acids and the corresponding aldehyde acids or their oxidation products were obtained. Of the esters of the unsaturated acids, triolein,[7] ricin-

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[1] This communication is an abstract of a portion of a thesis submitted by C. R. Noller in partial fulfilment of the requirements for the Degree of Doctor of Philosophy in Chemistry at the University of Illinois.

[2] (a) Harries and Thieme, *Ann.*, **343**, 354 (1905); *Ber.*, **39**, 2844 (1906). (b) Molinari and Soncini, *Ber.*, **39**, 2735 (1906). (c) Harries, *Ber.*, **39**, 3728 (1906). (d) Harries and Turk, *Ber.*, **39**, 3732 (1906). (e) Molinari and Barosi, *Ber.*, **41**, 2794 (1908). (f) Harries and Franck, *Ann.*, **374**, 356 (1910). (g) See also Brit. pat. 11,165, **1901**.

[3] (a) Thieme, *Inaug. Diss.*, Kiel, **1906**. (b) Noorduyn, *Rec. trav. chim.*, **38**, 317 (1919).

[4] Erdmann, Bedford and Raspe, *Ber.*, **42**, 1334 (1909).

[5] Ref. 3 a. Holde and Zadek, *Ber.*, **56**, 2052 (1923).

[6] Majima, *Ber.*, **42**, 674 (1909).

[7] Molinari and Fenaroli, *Ber.*, **41**, 2789 (1908).

olein,[3b] methyl and ethyl-oleates,[12] methyl ricinoleate,[8] methyl and ethyl linolenates[4] and methyl undecylenate,[9] have been ozonized. However, the procedures used seldom resulted in clear-cut reactions taking place. In the few instances where the melting points of the aldehyde acids were given[2d,8,3b] the different investigators obtained widely different values, and in only a single instance[8] was an aldehyde ester obtained for which a boiling point was reported. Generally, a complex mixture was obtained and the aldehyde acid or ester was identified by means of derivatives. In no case could the methods be called satisfactory for the preparation of these aldehyde acids or esters.

In this investigation the ozonation was carried out in glacial acetic acid. The special precaution that was necessary was in the decomposition of the ozonide. This must take place in the presence of a sufficient amount of zinc to prevent oxidation of the aldehydes formed; too small a quantity led invariably to a high-boiling fraction which consisted of the acid ester.

The three aldehydes prepared were methyl η-aldehydo-octanoate I from methyl oleate, methyl θ-aldehydo-nonanoate II,[10] from methyl undecylenate, methyl λ-aldehydo-dodecanoate III from methyl erucate.

$$CH_3\text{-}(CH_2)_7\text{-}CH{=}CH\text{-}(CH_2)_7\text{-}CO_2CH_3 \longrightarrow CH_3\text{-}(CH_2)_7\text{-}CHO + \underset{\text{I}}{CHO\text{-}(CH_2)_7\text{-}CO_2CH_3}$$

$$CH_2{=}CH\text{-}(CH_2)_8\text{-}CO_2CH_3 \longrightarrow HCHO + \underset{\text{II}}{CHO\text{-}(CH_2)_8\text{-}CO_2CH_3}$$

$$CH_3\text{-}(CH_2)_7\text{-}CH{=}CH\text{-}(CH_2)_{11}\text{-}CO_2CH_3 \longrightarrow CH_3\text{-}(CH_2)_7\text{-}CHO + \underset{\text{III}}{CHO\text{-}(CH_2)_{11}\text{-}CO_2CH_3}$$

It was observed that all of the aldehyde esters readily oxidized to the corresponding acid esters on standing in the air, particularly the aldehyde ester from methyl erucate. It was also noticed in the case of the aldehyde ester from methyl oleate that each time the product was distilled a residue remained. Upon examination this proved to be a trimer which could be depolymerized by heating to a high temperature and which could be saponified to the trimeric acid. It seems probable that the by-products obtained by some of the early investigators[2b,2d,2e,7] in the ozonation of some of the unsaturated acids consisted of polymers of the aldehyde acids.

To determine how easily acids of high molecular weight may be made from the aldehyde esters, *n*-butylmagnesium bromide was condensed with methyl η-aldehydo-octanoate. The hydroxy ester, methyl θ-hydroxy-

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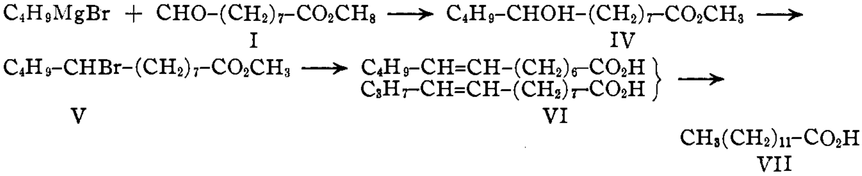
[8] Haller and Brochet, *Compt. rend.*, **150,** 496 (1910).

[9] Harding, Walsh and Weizmann, *J. Chem. Soc.*, **99,** 448 (1911).

[10] The isolation of the methyl θ-aldehydo-nonanoate in good yields by the ozonation of methyl undecylenate confirms previous work on the position of the double bond and gives added evidence that the views of Simon [*Compt. rend.*, **180,** 833 (1925)] concerning the structure of undecylenic acid are incorrect.

tridecanoate IV was obtained in about 35% yields.[11] Although the low- and high-boiling fractions from the reaction product were not investigated further, it was shown that no part of the product was unsaponifiable and therefore no Grignard reagent reacted with the ester group of the original aldehyde ester.

The methyl θ-hydroxy-tridecanoate IV was readily converted into tridecanoic acid VII in good yields by the following procedures: (a) the methyl θ-bromotridecanoate V was formed from the hydroxy ester by the action of phosphorus tribromide; (b) the methyl θ-bromotridecanoate was heated with alcoholic potassium hydroxide and converted probably into a mixture of olefinic acids VI; (c) the olefinic acids were reduced in alcohol solution with platinum-oxide platinum black and hydrogen to tridecanoic acid VII.



$$C_4H_9MgBr + \underset{I}{CHO\text{-}(CH_2)_7\text{-}CO_2CH_3} \longrightarrow \underset{IV}{C_4H_9\text{-}CHOH\text{-}(CH_2)_7\text{-}CO_2CH_3} \longrightarrow$$

$$\underset{V}{C_4H_9\text{-}CHBr\text{-}(CH_2)_7\text{-}CO_2CH_3} \longrightarrow \underset{VI}{\left.\begin{matrix} C_4H_9\text{-}CH{=}CH\text{-}(CH_2)_6\text{-}CO_2H \\ C_3H_7\text{-}CH{=}CH\text{-}(CH_2)_7\text{-}CO_2H \end{matrix}\right\}} \longrightarrow \underset{VII}{CH_3(CH_2)_{11}\text{-}CO_2H}$$

This same procedure is now being used to synthesize and to prove the constitution of a number of hydroxy and unsubstituted acids.

It is of interest that the melting point found for tridecanoic acid was 42–42.5° (corr.) which checks that reported by Le Seur[11a]. Levine reports 44.5–45.5°. This latter is higher than that given by Le Seur or in the present communication, probably because the author raised the temperature of the bath more rapidly than is customary.

Experimental Part

Ozonation of Unsaturated Esters. General Procedure: Preparation of Methyl η-Aldehydo-octanoate, Methyl θ-Aldehydo-nonanoate and Methyl λ-Aldehydo-dodecanoate.—A mixture of air and ozone[12] was bubbled through a solution of 0.5 mole of unsaturated ester in 300 cc. of glacial acetic acid until the solution no longer decolorized a solution of bromine in glacial acetic acid. By this time about three-quarters of the acetic acid had been carried away by the air. The remaining liquid was diluted with 400 cc. of ether and placed in a 3-liter flask fitted with a mechanical stirrer and reflux condenser. Stirring was started and 10 g.

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[11] Other hydroxy esters to be reported later have been prepared from simple aliphatic bromides and aldehyde esters with yields higher than 35%.

[11a] Le Seur, *J. Chem. Soc.*, **87**, 1905 (1905). Levine, West, Allen and Van der Scheer, *J. Biol. Chem.*, **23**, 71 (1915).

[12] In this investigation a commercial laboratory ozone machine was used which delivered about 5 g. of ozone per hour when air was passed through at the rate of 7 liters per minute. This method of ozonizing has been used by Helferich and Schäfer [*Ber.*, **57**, 1913 (1924)] for preparing certain hydroxy-aldehydes from hydroxy-olefines.

of zinc dust added together with 0.5 cc. of water, then 90 g. more of zinc in small portions. Finally, 10 cc. more of water was slowly added. The rate at which the zinc dust and water may be added depends on how vigorously the decomposition takes place, and cooling may at times be necessary. After the addition of zinc and water, the mixture was refluxed until it no longer gave a blue color when a drop was shaken with starch-potassium iodide solution. The zinc acetate sludge was then filtered through a Büchner funnel and washed thoroughly with ether. The original filtrate and ether washings were shaken twice with 500cc. portions of water, once with 200 cc. of 10% sodium carbonate solution, then with water and finally dried over calcium chloride. After distilling the ether, the residue was distilled under diminished pressure. The pelargonic aldehyde came over first, then the aldehyde ester and last a high-boiling fraction. The first fractionation gave a yield of 65–70% of aldehyde ester boiling over 10°. After a second fractionation a yield of 55–60% of aldehyde ester boiling over 5° was obtained.

TABLE I

ALDEHYDE ESTERS

	Unsatd. ester	Aldehyde ester	B. p., °C. (3 mm.) (corr.)	n_D^{20}	d_4^{20}
1.	Methyl oleate	$CHO-(CH_2)_7-CO_2CH_3$	111–112	1.4384	0.9704
2.	Methyl undecylenate	$CHO-(CH_2)_8-CO_2CH_3$	120–121	1.4410	.9663
3.	Methyl erucate[13]	$CHO-(CH_2)_{11}-CO_2CH_3$	152–153 (m. p., 19–20°)	1.4469	.9399

ANALYSES

	Subs., g.	CO_2, g.	H_2O, g.	Calcd., %		Found, %	
				C	H	C	H
1.	0.1664	0.3947	0.1476	64.47	9.73	64.69	9.86
2.	.1640	.3955	.1484	65.97	10.10	65.77	10.05
3.	.1893	.4821	.1837	69.37	10.82	69.46	10.78

An insufficient amount of zinc in the decomposition of the ozonides caused larger high fractions to appear. These were shown to contain the corresponding acid esters which will be described later.

Semicarbazones of Aldehyde Esters.—The semicarbazones were prepared by shaking equal weights of the aldehyde ester and semicarbazine sulfate with twice the weight of sodium acetate in dil. alcohol. The products crystallized and were purified from ethyl acetate.

TABLE II

SEMICARBAZONES OF ALDEHYDE ESTERS

Formula	M. p. °C. (corr.)	Analyses			
		Subs.	Cc. of N_2	Calcd., %	Found, %
$NH_2CONHN=CH-(CH_2)_7-CO_2CH_3$	104–105	0.1281	21.1 (28°, 745.6 mm.)	17.27	17.63
$NH_2CONHN=CH-(CH_2)_8-CO_2CH_3$	98–100 (94–96: lit., Ref. 9)	....	....	...	...
$NH_2CONHN=CH-(CH_2)_{11}-CO_2CH_3$	116.5–117.5	0.1800	24.0 (27°, 741.3 mm.)	14.04	14.25

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[13] Toyama, *J. Chem. Ind. Japan*, **25**, 1053 (1922).

Trimer of Methyl η-Aldehydo-octanoate.—On redistilling methyl η-aldehydo-octanoate which had stood for some time in an atmosphere of carbon dioxide or nitrogen, a residue of non-volatile material was obtained which solidified on cooling. When crystallized from petroleum ether (40–50°) to constant melting point, a white crystalline product resulted which melted at 34–36° (corr.). Analysis and molecular-weight determinations showed this to be the trimer of methyl η-aldehydo-octanoate.

Anal. Subs., 0.1688: CO_2, 0.3976; H_2O, 0.1484. Calcd. for $C_{30}H_{54}O_9$: C, 64.47; H, 9.73. Found: C, 64.24; H, 9.83.

Mol. wt. (cryoscopic method; solvent, benzene). Subs., 0.9311, 0.5496: C_6H_6, 16.735, 19.323; Δt, 0.550, 0.270. Calcd. for $C_{30}H_{54}O_9$, mol. wt., 516.4. Found: 506, 526.

If the trimer was heated under a pressure of 3 mm. to a temperature about 200° above the boiling point of the aldehyde ester, a yellow liquid slowly distilled, the temperature of the vapor being about 130°. This distillate gave a test for aldehyde with fuchsin-aldehyde reagent, and was presumably the aldehyde ester.

Trimer of η-Aldehydo-octanoic Acid.—Saponification of the trimeric aldehyde ester with alcoholic sodium hydroxide gave an acid which was purified by crystallization from acetone. It formed white crystals melting at 112–113° (corr.).

Anal. Subs., 0.1947, 0.3602: CO_2, 0.4460; H_2O, 0.1677; 19.32 cc. of 0.1079 *N* KOH. Calcd. for $C_{27}H_{48}O_9$: C, 62.75; H, 9.36; neutr. equiv., 172.1. Found: C, 62.48; H, 9.57; neutr. equiv., 173.3.

Monomethyl Esters of Azelaic, Sebacic and Brassylic Acids.—The aldehyde esters oxidized very readily in the air to the corresponding acid esters. They could also be isolated from the high-boiling fraction in the distillation of the aldehyde esters by extraction with alkali. When too little zinc had been used in decomposition of the ozonides, they were present in very appreciable quantities. The monomethyl sebacate and monomethyl brassylate solidified readily after cooling and standing and were purified by recrystallization from petroleum ether (40–50°). The monomethyl azelate solidified only when cooled to a low temperature and was purified best by distillation under diminished pressure.

TABLE III

MONOMETHYL AZELATE, SEBACATE AND BRASSYLATE

	Acid ester	M. p., °C. (corr.)	Subs.	Cc. of 0.0842 *N* KOH	Neut. equiv. Calcd.	Neut. equiv. Found
1.	$HO_2C-(CH_2)_7-CO_2CH_3$	22–24° (b. p. 158.5–159.5° at 3 mm.)[a]	0.4299	24.76	202.1	206.2
2.	$HO_2C-(CH_2)_8-CO_2CH_3$	40–41	.4568	25.04	216.2	216.7
3.	$HO_2C-(CH_2)_{11}-CO_2CH_3$	57–57.5	.5125	23.63	258.2	257.6

[a] n_D^{25}, 1.4451; d_4^{25}, 1.0348.

ANALYSES

	Subs., g.	CO_2, g.	H_2O, g.	Calcd., % C	Calcd., % H	Found, % C	Found, % H
1.	0.1880	0.4104	0.1536	59.38	8.96	59.54	9.08
2.	.1691	.3778	.1443	61.05	9.34	60.91	9.48
3.	.1745	.4189	.1641	65.07	10.15	65.46	10.45

Upon saponification, the three acid esters yield, respectively, azelaic acid, m. p. 106–106.5°, sebacic acid, m. p. 133–134° and brassylic acid, m. p. 112–113°.

Condensation of Aldehyde Esters with Grignard Reagents. Preparation of Methyl θ-Hydroxy-tridecanoate IV.—A solution of 0.2 mole of freshly distilled aldehyde ester in 200–300 cc. of absolute ether was cooled to —5° in a flask fitted with a mechanical stirrer, a condenser closed with a calcium chloride tube, a thermometer and a separatory funnel. To this was added through the separatory funnel during rapid stirring a solution of the Grignard reagent prepared from 0.2 mole of alkyl bromide in 200 cc. of ether, while the temperature was kept between —5° and 0°. The condensation product immediately began to precipitate and formed a heavy, sticky mass on the sides of the flask. After all the Grignard reagent had been added, the mixture was allowed to stand in an ice-water bath for two hours, the ether layer poured off and the residue decomposed with a solution of 50 g. of ammonium chloride in 500 cc. of water. The resulting oil was extracted with ether and the ether solution washed with 1:10 hydrochloric acid, then with water, and dried over anhydrous magnesium sulfate. After evaporation of the ether, the residue was fractionally distilled under diminished pressure. A low- and a high-boiling fraction were obtained, boiling from 40° to 50° apart, the higher of which consisted of the desired hydroxy ester; a non-volatile residue also resulted.

From butylmagnesium bromide prepared from 27.4 g. of *n*-butyl bromide and 37.2 g. of methyl η-aldehydo-octanoate was obtained 18.5 g. (38%) of methyl θ-hydroxy-tridecanoate boiling over 5°. On redistillation it boiled at 154–155° (3 mm.); n_D^{20}, 1.4490; d_4^{20}, 0.9316.

Anal. Subs., 0.1721: CO_2, 0.4331; H_2O, 0.1785. Calcd. for $C_{14}H_{28}O_3$: C, 68.79; H, 11.55. Found: C, 68.63; H, 11.52.

θ-Hydroxy-tridecanoic Acid.—This acid was obtained by saponification with alcoholic potassium hydroxide. It was purified by repeated crystallization from acetone, forming white crystals; m. p., 49–51° (corr.).

Anal. Subs., 0.1830, 0.4216: CO_2, 0.4555; H_2O, 0.1887; 16.96 cc. of 0.1079 *N* KOH. Calcd. for $C_{13}H_{26}O_3$: C, 67.78; H, 11.38; neutr. equiv., 230.2. Found: C, 67.88; H, 11.46; neutr. equiv., 230.4.

Preparation of Tridecanoic Acid from Methyl θ-Hydroxy-tridecanoate.—To 0.03 mole of hydroxy ester was added during stirring 0.015 mole of redistilled phosphorus tribromide. The mixture was stirred for one-half hour at room temperature, then for one-half hour on the steam cone, and finally decomposed with water, washed with 10% sodium carbonate solution and water, and extracted with ether. The combined extracts were dried over magnesium sulfate and the ether was evaporated. The bromide decomposed on distillation at 3 mm. pressure so that the crude bromide was converted into the unsaturated acid by refluxing for four hours with a solution of 10 g. of potassium hydroxide in 50 cc. of 95% alcohol. After dilution with water and evaporation of most of the alcohol, the solution was acidified, extracted twice with ether, and the ether extracts were dried over magnesium sulfate. On evaporation of the ether, an oil remained, which was dissolved in 50 cc. of 95% alcohol and reduced with hydrogen at 2 to 3 atmospheres pressure in the presence of 0.15 g. of platinum-oxide platinum black catalyst. Slightly less than the calculated quantity of hydrogen was absorbed in about two minutes. After the catalyst had been filtered off, the alcohol was diluted to slight turbidity and cooled in an ice-salt mixture when the saturated acid crystallized. The acid was easily purified by crystallization from 70% alcohol and then from petroleum ether (40–50°). From 18.3 g. of methyl θ-hydroxy-tridecanoate was obtained 9.5 g. (60%) of tridecanoic acid. When pure, it formed white crystals; m. p., 42–42.5° (corr.).

Anal. Subs., 0.4156: 22.90 cc. of 0.0842 *N* KOH. Calcd. for $C_{13}H_{26}O_2$: neutr. equiv., 214.2. Found: 215.5.

Summary

1. A satisfactory method is given for preparing various aldehyde esters by the ozonation of the methyl esters of unsaturated acids.
2. The use of the aldehyde esters in synthesizing hydroxy acids and unsubstituted acids is illustrated by the conversion of methyl η-aldehydo-octanoate by means of butylmagnesium bromide into methyl θ-hydroxy-tridecanoate and, finally, conversion of this latter compound through the bromide and olefinic acid to tridecanoic acid.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

SYNTHESIS OF DIHYDROCHAULMOOGRIC AND DIHYDROHYDNOCARPIC ACIDS. II

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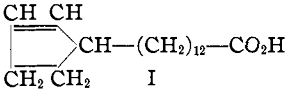
In a recent paper by Shriner and Adams[2] a careful consideration of the experimental work of Power[3] and collaborators together with the consideration of new experimental evidence led to the conclusion that chaulmoogric and hydnocarpic acids were not tautomeric substances but that all the reactions of these two compounds could be explained by one structural formula for each; chaulmoogric acid I; hydnocarpic acid II.



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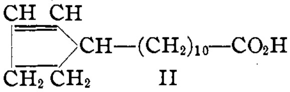
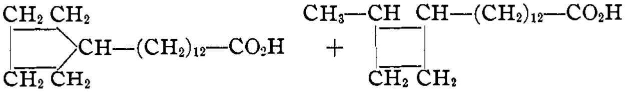
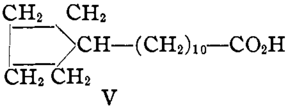


II

By reduction of the hydrogen bromide addition compound of chaulmoogric acid, Power[3c] obtained a dihydrochaulmoogric acid which he regarded as a mixture of μ-cyclopentyl-tridecanoic acid III and 2-methyl-μ-cyclobutyl-tridecanoic acid IV.



III IV



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[1] This communication is an abstract of a portion of a thesis submitted by C. R. Noller in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry at the University of Illinois.

[2] Shriner and Adams, THIS JOURNAL, **47**, 2727 (1925).

[3] Power and Gornall, (a) *J. Chem. Soc.*, **85**, 838 (1904); (b) **85**, 851 (1904). (c) Barrowcliff and Power, *ibid.*, **91**, 557 (1907).