and so that the hydrolysis product would be comparable for an infrared absorption study to that obtained by direct synthesis. A mixture of 2-*n*-amyl-2-methyl-4-(3',5'-dinitrobenzoxymethyl)-1,3-dioxolane (9.7 g., 0.25 mole), potassium hydroxide (2.8 g.) and water (100 ml.) was boiled gently for one hour. The basic solution was dried, the ether was removed, and the residual oil was distilled yielding 3.0 g. (62.5%) of a colorless oil; b. p. 70–72° at 0.5 mm., $n^{21}D$ 1.4468, $d^{21}$ 0.988. These physical properties and the infrared absorption spectra of this compound (see Fig. 1) are essentially identical with those obtained for the product from the direct reaction of methyl *n*-amyl ketone and glycerol.

### Evidence for the Structure of the Condensation Product of Glycerol and Heptanal

**(A) Treatment of the Condensation Product with Trityl Chloride in Pyridine.**—The condensation product was treated with trityl chloride in anhydrous pyridine according to the procedure of Seikel and Huntress.[23] The reaction mixture was heated on the steam-bath for five minutes. From 18.8 g. of condensation product there was obtained, after one crystallization from alcohol, 26.0 g. (58%) of white crystals, m. p. 56–58°. This crude material apparently represents a mixture of the diastereoisomeric racemates, which are possible for 2-*n*-hexyl-4-(triphenylmethoxymethyl)-1,3-dioxolane. By repeated recrystallization of this material from alcohol a pure sample of white crystals, m. p. 70–71°, was obtained.

*Anal.* Calcd. for $C_{29}H_{34}O_3$: C, 80.93; H, 7.90. Found: C, 81.03; H, 7.81.

**(B) Preparation of a Sample of 2-*n*-Hexyl-4-hydroxymethyl-1,3-dioxolane of Known Structure**

**2-*n*-Hexyl-4-(3',5'-dinitrobenzoxymethyl)-1,3-dioxolane.**—A mixture of 25.0 g. of 3-(3',5'-dinitrobenzoxy)-1,2-propanediol,[24] 18.2 g. of heptanal and 80 ml. of benzene was heated in a flask connected to an ordinary water-eliminator. When the expected quantity of water had separated, the benzene was removed and the residue was triturated with hexane. The fluffy, white crystals, m. p. 65–68°, which separated, were collected on a filter and weighed 16.0 g. (48%). Since this crude material probably represents a mixture of the two possible diastereoisomeric racemates, it was employed without further purification in the hydrolysis experiment described below. Repeated recrystallization of the crude material from a mixture of benzene and hexane gave a pure sample of one of the racemates, m. p. 74–75°.

*Anal.* Calcd. for $C_{17}H_{22}N_2O_8$: C, 53.41; H, 5.76. Found: C, 53.43; H, 5.67.

**2-*n*-Hexyl-4-hydroxymethyl-1,3-dioxolane.**—A mixture of 14.0 g. of the crude 2-*n*-hexyl-4-(3',5'-dinitrobenzoxymethyl)-1,3-dioxolane, m. p. 65–68°, and 90 ml. of a 5% potassium hydroxide solution was boiled under reflux for three hours. The organic layer was then extracted with ether, washed, dried, and the ether was removed. Distillation of the residue yielded 4.0 g. (58%) of a colorless oil; b. p. 80° at 0.2 mm.; $n^{21}D$ 1.4492; $d^{21}$ 0.988; *M* calcd. 50.92; $M_{obsd.}$ 51.05.

*Anal.* Calcd. for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71. Found: C, 63.83; H, 10.78.

## Summary

Some substituted dioxolanes, dioxaspiranes and dithiolanes of possible interest as agents for effecting muscular paralysis have been prepared. On the basis of chemical evidence and infrared absorption spectra data, the condensation products of glycerol with methyl *n*-amyl ketone and methyl *n*-hexyl ketone have been assigned the structures of 2,2-dialkyl-4-hydroxymethyl-1,3-dioxolanes.

On the basis of similar evidence the condensation product of glycerol and heptanal is thought to be a mixture of which the predominant constituent is 2-*n*-hexyl-4-hydroxymethyl-1,3-dioxolane.

ROCHESTER, NEW YORK RECEIVED FEBRUARY 21, 1949

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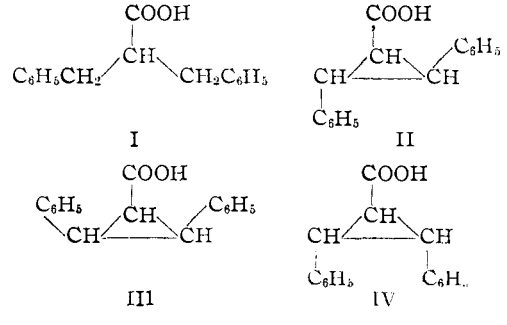
[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

# Analogs of Dibenzylacetic Acid[1]

BY ALFRED BURGER, DIETER G. MARKEES,[2] WILLIAM R. NES[3] AND WILLIAM L. YOST[4]

Certain dialkylaminoalkyl esters of dibenzylacetic acid abolish spasm produced by barium chloride or histamine several times as effectively as papaverine while their atropine-like activity against spasm caused by acetylcholine is generally low.[5] A comparison of analogous compounds in which the benzyl groups have been altered by cyclization or isosteric replacements promised to clarify further this relationship.

The first of our variations of the structure of dibenzylacetic acid (I) was concerned with a steric fixation of the two benzyl carbon atoms by incorporating them in a cyclopropane ring. The required 2,3-diphenylcyclopropanecarboxylic acids were prepared by adding ethyl diazoacetate to *cis*- and *trans*-stilbene, respectively, decomposing the intermediate pyrazoline derivative without isolation, and hydrolyzing the resulting esters. *trans*-Stilbene gave only one racemic acid (II), and only one of the two meso forms (III and IV) expected from *cis*-stilbene could be isolated from the reaction mixture. For further comparison, 2,2-diphenylcyclopropanecarboxylic acid (V) was



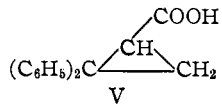

(1) Presented in part before the 114th Meeting of the American Chemical Society, Washington, D. C., August 31, 1948.

(2) Charles C. Haskell Postdoctorate Fellow, 1947.

(3) Du Pont Senior Fellow, 1948.

(4) Smith, Kline and French Fellow, 1947.

(5) Wagner-Jauregg, Arnold and Born, *Ber.*, **72**, 1551 (1939).

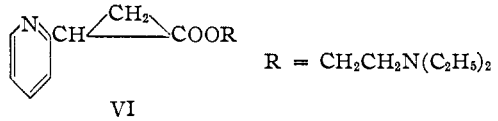


V

prepared from ethyl diazoacetate and 1,1-diphenylethylene.[6] The yields of the cyclopropane derivatives were low in all these cases, perhaps because of the aromatic character of the extracyclic double bond of the starting materials.

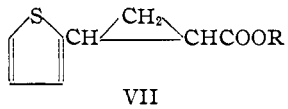
Dialkylaminoalkyl esters of the diphenylcyclopropanecarboxylic acids were prepared where the supply permitted.

We had available in this Laboratory 2-phenylcyclopropanecarbonyl chloride,[7] and converted it to the diethylaminoethyl ester. In an analogous manner, diethylaminoethyl 2-(2-pyridyl)- and 2-(2-thienyl)-cyclopropanecarboxylates were prepared (VI and VII). The acid moieties of these esters were obtained from ethyl diazoacetate and 2-vinylpyridine, and 2-vinylthiophene, respectively, by a series of reactions described for the phenyl prototype.[7]



R = $CH_2CH_2N(C_2H_5)_2$

VI



VII

In order to avoid the formation of stereoisomeric mixtures of these heterocyclic cyclopropanecarboxylic acids, purification through the acid chloride was chosen in each case. Basic esters were prepared from the chlorides and diethylaminoethanol.

This series was not further investigated when a basic ester of 2-phenyl-2-methyl-cyclopropanecarboxylic acid was described recently.[8]

Another approach to analogs of antispasmodics of the dibenzylacetic acid type was sought among basic esters (VIIIa) and amides (VIIIb) of diphenoxyacetic acid.

$(C_6H_5O)_2CHCOR$ VIII

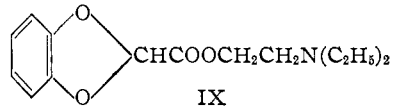
R = (a) $O(CH_2)_nNR_2$
(b) $NH(CH_2)_nNR_2$
(c) Cl

In these compounds, the oxygen atoms replace the isosteric methylene groups of the benzyl radicals. Since diphenoxyacetic acid is the diphenyl acetal of glyoxylic acid and is attacked readily by hydrolytic agents, it was considered possible that esters of the formula VIIIa may exert a short-lived antispasmodic activity which would give place to the antiseptic effect of phenol as the latter is liberated in analogy to Nencki's salol principle.

The preparation of these derivatives offered no difficulty. Diphenoxyacetyl chloride (VIIIc), prepared from the acid and thionyl chloride,[9] reacted smoothly with aminoalcohols and aminoalkyl dialkylamines. The resulting basic esters and amides could not be distilled without decomposition but were isolated as salts or hydrates. They were colorless substances most of which did not crystallize without some effort. Although stable for limited periods of time, they decomposed slowly after several months with a distinct odor of phenol.

It would have been shorter to prepare these basic esters from ethyl diphenoxyacetate by base-catalyzed ester interchange[10] but the materials decomposed at the high temperature of the reaction.

A much lower degree of stability was displayed by diethylaminoethyl *o*-phenylenedioxyacetate (IX) which decomposed in a sealed dark vessel within a few hours and could not be identified by analysis. It shares this instability with phenylenedioxyacetic acid and its simple alkyl esters which are easily hydrolyzed even by dilute alkali.



IX

**Pharmacological Observations.**—Several of the dialkylaminoalkyl esters described in this paper have been tested by Dr. E. J. Fellows. He reports that none of the phenylacetal-type esters exhibited antispasmodic activity in concentrations of $1 \times 10^{-6}$ when tested by the isolated intestinal strip method. Only γ-(2-methylpiperidino)-propyl diphenoxyacetate hydrochloride protected guinea pigs from bronchospasm produced by aerosolized histamine in doses devoid of side effects. Several esters of this series (diethylaminoethyl, morpholinoethyl, and γ-(2-methylpiperidinopropyl)), as well as β-morpholinoethyl diphenoxyacetamide caused local anesthesia of a low order for 7.6 to 16.3 minutes when applied topically to rabbits' eyes in a 1% concentration but all of them showed signs of irritation. The same held true for β-diethylaminoethyl 2-phenylcyclopropanecarboxylate.

**Acknowledgment.**—We are grateful to Smith, Kline and French Laboratories for support of this work, and to Dr. E. J. Fellows of this Company for the pharmacological tests.

## Experimental[11]

**2-Aryl- and 2-Heteroarylcyclopropane-1-carboxylic Acids and Derivatives. General Procedures.**—A mixture of 0.1 mole of the ethylene derivative and 0.1 mole of ethyl diazoacetate, and usually about two volumes of xylene was warmed to 120–130° until evolution of nitrogen began. The reaction proceeded exothermically except in the case of 1,1-diphenylethylene, and was completed by refluxing until no more gas was evolved. The solvent was

(6) Wieland and Probst, *Ann.*, **530**, 274, 289 (1937).
(7) Burger and Yost, THIS JOURNAL, **70**, 2198 (1948).
(8) Tilford, Van Campen and Shelton, *ibid.*, **69**, 2902 (1947).
(9) Scheibler and Baumann, *Ber.*, **62**, 2057 (1929).
(10) Holmes, U. S. Patent 2,399,736 (1946); Hill and Holmes, U. S. Patent 2,394,770 (1946).
(11) All melting points are corrected. Many of the microanalyses have been performed by Clark Microanalytical Laboratory, Urbana, Illinois.

TABLE I

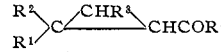
PREPARATION OF SUBSTITUTED CYCLOPROPANECARBOXYLIC ACIDS

| Starting ethylene derivative | Ethyl ester of cyclopropane-carboxylic acid formed | Solvent used | Heating, hours | Yield, %, ethyl ester | Hydrolysis, hours | Yield, %, crude acid based on olefin |
|---|---|---|---|---|---|---|
| 2-Vinylthiophene | 2-(2-Thienyl) | Xylene | 1 | 76 | 6.5 | 72 |
| 2-Vinylpyridine | 2-(2-Pyridyl) | Xylene | 0.5 | 63 | 10[a] | 60 |
| *trans*-Stilbene | 2,3-Diphenyl[b] | .... | 0.5 | .. | 3 | 5 |
| *cis*-Stilbene | 2,3-Diphenyl[b] | | 0.25 | .. | 3 | 5 |
| 1,1-Diphenylethylene | 2,2-Diphenyl | Xylene | 4 | 6.7 | 3 | 4.5 |

[a] Hydrolysis in concentrated hydrochloric acid. [b] The ester was not fractionated, the reaction mixture was saponified, and the carboxylic acid separated from non-acidic products.

TABLE II

PHYSICAL PROPERTIES AND ANALYSES OF SUBSTITUTED CYCLOPROPANECARBOXYLIC ACIDS AND DERIVATIVES

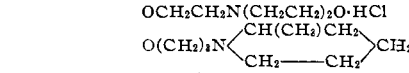


| R' | $R^2$ | $R^3$ | $R^4$ | Appearance[i] | Crystn. solvent | M. p. or b. p., °C. | Mm. | Formula | Percentage composition Calcd. | Found | Calcd. | Found |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $C_6H_5$ | H | H | $OC_2H_4NEt_2$ | Oil | | 161 | 4.4 | $C_{16}H_{23}NO_2$ | C, 73.53 | 73.26 | H, 8.87 | 8.60 |
| | | | | | | 156 | 3.1 | | | | | |
| $C_4H_3S$[a] | H | H | $OC_2H_5$ | Y. oil[b] | | 107 | 3 | $C_{16}H_{12}O_2S$ | ..... | .... | ..... | .. |
| $C_4H_3S$[a] | H | H | OH | Nd. | $H_2O$ | 124–125 | | $C_8H_8O_2S$ | Mol. wt. 168.2 | 169.3 | ..... | .. |
| $C_4H_3S$[a] | H | H | $NH_2$ | Lf. | $H_2O$ | 163–164 | | $C_8H_9NOS$ | N, 8.38 | 8.28 | ..... | .. |
| $C_4H_3S$[a] | H | H | $NHC_6H_5$ | Nd. | $C_6H_6$–pet. eth. | 119 | | $C_{14}H_{13}NOS$ | N, 5.76 | 5.67 | ..... | .. |
| $C_4H_3S$[a] | H | H | $OC_2H_4NEt_2$ | Y. oil | | 161 | 2.5 | $C_{14}H_{21}NO_2S$ | N, 5.24 | 5.24 | ..... | .. |
| $C_5H_4N$[c] | H | H | $OC_2H_5$ | Y. oil | | 116 | 3 | $C_{11}H_{13}NO_2$ | N, 7.33 | 7.30 | ..... | .. |
| $C_5H_4N$[c] | H | H | $OC_2H_5$ (picrate) | Y. nd. | EtOH | 122–124 | | $C_{17}H_{16}N_4O_9$ | N, 13.33 | 13.28 | ..... | .. |
| $C_5H_4N$[c] | H | H | OH | Prisms | $C_6H_6$–pet. eth. | 98–100 | | $C_9H_9NO_2$ | N, 8.58 | 8.41 | ..... | .. |
| $C_5H_4N$[c] | H | H | $OC_2H_4NEt_2$ | Y. oil | | 162–163 | 2 | $C_{18}H_{22}N_2O_2$ | N, 10.68 | 10.38 | ..... | .. |
| $C_6H_5$ | H | $C_6H_5$[d] | OH[e] | Nd. | EtOH–$H_2O$ | 153–154 | | $C_{15}H_{14}O_2$ | C, 80.65 | 80.21 | 5.92 | 6.00 |
| $C_6H_5$ | H | $C_6H_5$[d] | $NH_2$[e] | Nd. | EtOH–$H_2O$ | 126.5–127.5 | | $C_{15}H_{15}NO$ | N, 5.90 | 5.82 | ..... | .. |
| $C_6H_5$ | H | $C_6H_5$[d] | $NHC_6H_5$ | Nd. | EtOH–$H_2O$ | 191–191.5 | | $C_{22}H_{19}NO$ | N, 4.47 | 4.71 | ..... | .. |
| $C_6H_5$ | H | $C_6H_5$[d] | $OC_2H_4NEt_2 \cdot HCl$ | Powder | EtOAc | 185–188 | | $C_{22}H_{28}ClNO_2$ | N, 3.75 | 3.82 | ..... | .. |
| $C_6H_5$ | H | $C_6H_5$[f] | OH | Oil[g] | | | | $C_{15}H_{14}O_2$ | ..... | .... | ..... | .. |
| $C_6H_5$ | H | $C_6H_5$[f] | $NH_2$ | Nd. | EtOH–$H_2O$ | 212–215 | | $C_{15}H_{15}NO$ | N, 5.90 | 5.68 | ..... | .. |
| $C_6H_5$ | $C_6H_5$ | H | $OC_2H_5$ | Y. oil[b] | | | | | ..... | .... | ..... | .. |
| $C_6H_5$ | $C_6H_5$ | H | OH | Nd. | Ether | 166–169[h] | | $C_{15}H_{14}O_2$ | C, 80.65 | 80.73 | 5.92 | 6.13 |
| $C_6H_5$ | $C_6H_5$ | H | $NH_2$ | Nd. | EtOH–$H_2O$ | 178.5–179.5 | | $C_{15}H_{15}NO$ | N, 4.47 | 4.56 | | |
| $C_6H_5$ | $C_6H_5$ | H | $NHC_6H_5$ | Nd. | EtOH | 222–223 | | $C_{22}H_{19}NO$ | N, 5.90 | 5.70 | | |

[a] 2-Thienyl. [b] This ester was not purified for analysis. [c] 2-Pyridyl. [d] *trans*-. [e] First prepared by J. W. Kuck. [f] *cis*-. [g] Neither *cis*-2,3-diphenylcyclopropanecarboxylic acid nor its ethyl ester could be obtained in the pure state. [h] Wieland and Probst[6] reported m. p. 171°. [i] y = yellow; nd = needles; lf = leaflets.

TABLE III

DERIVATIVES OF DIPHENOXYACETIC ACID, $(C_6H_5O)_2CHCOR$

| R | Crystn. solvent | M. p., °C. | Formula | Carbon, % Calcd. | Found | Hydrogen, % Calcd. | Found | Nitrogen, % Calcd. | Found |
|---|---|---|---|---|---|---|---|---|---|
| $N(CH_3)_2$[a] | 30% EtOH | 84–85 | $C_{16}H_{17}NO_3$ | ... | ... | .. | .. | 5.16 | 5.28 |
| $N(CH_2)_2NEt_2 \cdot HCl$[b] | EtOH–EtOAc | 64–65 | $C_{21}H_{29}ClN_2O_3$ | 64.19 | 63.57 | 7.44 | 7.61 | 7.13 | 7.21 |
| $N(CH_2)_2N(CH_2CH_2)_2O \cdot HCl$ | EtOAc | 146–148 | $C_{20}H_{25}ClN_2O_4$ | 61.14 | 60.89 | 6.37 | 6.58 | 7.13 | 7.00 |
| $OCH_2CH_2N(CH_3)_2 \cdot H_2O$ | EtOAc[c,d] | 108–110 | $C_{18}H_{23}NO_6$ | 64.86 | 64.78 | 6.90 | 6.99 | 4.20 | 4.11 |
| $OCH_2CH_2NEt_2 \cdot HCl$[e] | EtOAc | 144–145 | $C_{20}H_{26}ClNO_4$ | 63.26 | 63.15 | 6.85 | 6.87 | 3.68 | 3.67 |
| $OCH_2CH_2NC_5H_{10} \cdot HCl$[e] | EtOH–EtOAc | 134–136 | $C_{21}H_{26}ClNO_4$ | 64.35 | 64.05 | 6.69 | 6.62 | 3.57 | 3.52 |
| $OCH_2CH_2N(CH_2CH_2)_2O \cdot HCl$ | $C_6H_6$ | 105–106 | $C_{20}H_{24}ClNO_5$ | 60.98 | 60.33 | 6.14 | 6.09 | 3.56 | 3.61 |
|  | $C_6H_6$–$Et_2O$ | 79–84 | $C_{23}H_{30}ClNO_4$ | ... | ... | ... | ... | 3.52 | 3.34 |
| $O(CH_2)_2NEt_2 \cdot HCl$ | $C_6H_6$ | 115–117 | $C_{21}H_{28}ClNO_4$ | 64.03 | 62.63 | 7.16 | 7.23 | 3.56 | 3.83 |

[a] Needles. [b] Hygroscopic. [c] The hygroscopic hydrochloride was decomposed with bicarbonate solution, the base extracted into ether, and the solvent allowed to evaporate slowly at room temperature in order to give the hydrated material. [d] The anhydrous ester is liquid, b. p. 165–175° (3 mm., dec.). [e] Flakes. [f] The 3-(α-methylpiperidino)-propanol used in the preparation of this compound was kindly supplied by Eli Lilly & Co.

stripped and the remaining oil was fractionated. The esters were hydrolyzed by refluxing with 3 to 12% ethanolic sodium hydroxide solution for four to six hours, most of the ethanol was removed, non-acidic products were extracted into ether, and the substituted cyclopropanecarboxylic acids were precipitated with hydrochloric acid as solids, or oils which usually solidified soon.

The amphoteric 2-(2-pyridyl)-cyclopropanecarboxylic acid could be obtained by neutralization of the saponification mixture to *p*H 6.6 and continuous extraction with ether. Hydrolysis of the ester with concentrated hydrochloric acid, evaporation of the reaction mixture and recovery of the hydrochloride of the carboxylic acid was more advantageous.

Stereochemically homogeneous samples were produced by boiling the acids with thionyl chloride in benzene solution for two hours, and reconverting the acid chlorides to the acids by hydrolysis with hot water.[7]

The esters, amides and anilides of the acids were prepared from the acid chlorides in benzene solution by treatment with the corresponding reagent.

**Basic Esters and Amides of Diphenoxyacetic Acid.**—Eight parts of diphenoxyacetic acid[12] was refluxed in benzene solution with seven parts of purified thionyl chloride for six to seven hours, and the mixture was allowed to stand overnight. Benzene and thionyl chloride were stripped under reduced pressure, and the crude acid chloride[9] was used in the next step.

Equivalent amounts of diphenoxyacetyl chloride and the dialkylaminoalkanol, or dialkylaminoalkylamine, respectively, were mixed in benzene solution. After an initial exothermic reaction the hydrochlorides of the reaction products precipitated, and usually solidified after some standing. In selected cases, the bases were liberated with sodium bicarbonate solution, and purified if they were more readily handled than the salts.

**Isoamyl *o*-Phenylenedioxyacetate.**—The preparation of this ester was patterned on that reported for the ethyl ester.[13] The preparative modification described here produced the isoamyl ester in a yield of 16.7% as compared with 8% reported for the ethyl ester.[14]

To a hot solution of 106 g. of sodium in 1200 cc. of dry isoamyl alcohol was added a suspension of 254 g. of catechol in 250 cc. of isoamyl alcohol with stirring in an atmosphere of nitrogen. The resulting viscous white mass was heated at 120° and treated gradually with 362 g. of ethyl dichloroacetate at such a rate that the exothermic reaction subsided after about one-half of the ester had been added. The reaction mixture became fluid and turned purple. It was refluxed another sixteen hours, 700 cc. of isoamyl alcohol was distilled off at 20 mm. pressure, and the dark viscous residue was dissolved in 2 liters of ether. The ether solution was washed with several liters of an ice-cold calcium chloride solution, and then with two 500-cc. portions of cold 2% sodium hydroxide solution. The dark red ether layer was dried over calcium chloride, the solvent was distilled, and the residual oil was fractionated several times. The colorless fraction boiling finally at 149–152° (20 mm.) weighed 90 g. (16.7%). It consisted of practically pure isoamyl *o*-phenylenedioxyacetate but gave a weak test for catechol. Repeated fractionation to b. p. 122–124° (2 mm.) furnished a satisfactory analytical sample.

(12) Auwers and Haymann, *Ber.*, **27**, 2795 (1894).

(13) Christiansen and Dolliver, THIS JOURNAL, **66**, 312 (1944).

(14) Dolliver, private communication.

*Anal.* Calcd. for $C_{13}H_{16}O_4$: C, 66.10; H, 6.78. Found: C, 66.05; H, 7.00.

***o*-Phenylenedioxyacetic Acid.**—A mixture of 13 g. of isoamyl *o*-phenylenedioxyacetate and 75 cc. of 8% sodium hydroxide solution was heated at 90° for forty-five minutes; isoamyl alcohol was extracted with ether, and the colorless solution was acidified and extracted with ether. After drying over sodium sulfate, the solvent was removed, and the residual oil was allowed to crystallize from petroleum ether. The yield of colorless flakes, m. p. 104–106°, was 6 g. (65.6%). The material gave no ferric chloride test for catechol, and did not depress the melting point of an authentic sample[13].

***o*-Phenylenedioxyacetamide.**—When dry ammonia was passed through isoamyl *o*-phenylenedioxyacetate at 100°, the ester became cloudy, and the product cleared and solidified after thirty minutes. The colorless amide crystallized from ether–petroleum ether, m. p. 105–106°. It gave no color test with ferric chloride, and could be hydrolyzed with 25% sodium hydroxide solution at room temperature.

*Anal.* Calcd. for $C_8H_7NO_3$: N, 8.41. Found: N, 8.62.

The amide could also be prepared in poor yields, from *o*-phenylenedioxyacetyl chloride which was obtained from the acid and thionyl chloride in benzene solution. This acid chloride could not be purified but served also as the starting material for the preparation of the unstable diethylaminoethyl *o*-phenylenedioxyacetate.

## Summary

The condensation of several aromatically and heterocyclically substituted ethylene derivatives with ethyl diazoacetate furnished the ethyl esters of the corresponding cyclopropanecarboxylic acids. Dialkylaminoalkyl esters of some of these acids were prepared as potential antispasmodics.

A series of dialkylaminoalkyl diphenoxyacetates and diphenoxyacetamides was prepared for comparison with the isosteric derivatives of dibenzylacetic acid. The chemical stability of the acetal type derivatives of diphenoxyacetic acid was compared with that of similar compounds derived from *o*-phenylenedioxyacetic acid.

CHARLOTTESVILLE, VIRGINIA RECEIVED MARCH 23, 1949

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[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

# The Synthesis of Some 1-Cyclopentenealdehydes

BY JAMES ENGLISH, JR., AND GEORGE W. BARBER[1]

In many of the possible synthetic approaches[2] to molecules having structures analogous to auxin a[3] substituted 1-cyclopentenealdehydes are necessary starting materials. The preparation of such substances has therefore been undertaken with a view to their eventual utilization in a synthetic program.

1-Cyclopentenealdehyde itself has been prepared by the rearrangement of cyclohexene peroxide[4] and from adipic aldehyde obtained by ozonolysis of cyclohexene.[5] Urion obtained this substance also by treatment of divinylglycol with alumina at 300°.[6] These methods, however, are not easily adapted to the preparation of substituted 1-cyclopentenealdehydes and in our experience have given unsatisfactory yields. The process finally developed is shown in the equations.

The 3-*n*-propyl- and 3,5-di-*n*-propylpyrocatechols were prepared from the corresponding allyl derivatives by hydrogenation; the allyl pyrocate-

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