Anal. Calcd. for $C_{14}H_9O_2Cl$: C, 68.72; H, 3.71; Cl, 14.49. Found: C, 68.74; H, 3.90; Cl, 14.67.

3-(Bromophenyl)phthalide. Five grams (0.033 mole) of phthalaldehydic acid was dissolved in 30 ml. of 2:1 conc. sulfuric acid-20% fuming sulfuric acid. To this was added 5.23 g. (0.033 mole) of bromobenzene. Following essentially the same procedure outlined for the preparation of 3-(chlorophenyl)phthalide there was obtained 9.25 g. (96%) of crude product. Crystallization from ethanol yielded a white crystalline solid which did not show a sharp melting point but softened at 92° and finally became completely liquid *ca.* 105°, indicating a mixture of isomers. The reported[14] melting point for 3-(*p*-bromophenyl)phthalide is 139–140°.

Anal. Calcd. for $C_{14}H_9O_2Br$: C, 58.16; H, 3.14; Br, 27.64. Found: C, 58.32; H, 3.07; Br, 27.47.

3-(2,5-Dichlorophenyl)phthalide. Five grams (0.033 mole) of phthalaldehydic acid was dissolved in 36 ml. of 1:1 concentrated sulfuric acid-20% fuming sulfuric acid. To this was added 4.9 g. (0.033 mole) of *p*-dichlorobenzene. In order to keep the insoluble *p*-dichlorobenzene in melted condition the reaction vessel was placed in a water bath maintained at 65–70°. The mixture was mechanically stirred, and after about 2 hr. the dispersed *p*-dichlorobenzene disappeared, yielding a homogeneous reddish-brown solution. The mixture was allowed to stand in the hot water bath for an additional hour, then cooled and poured slowly with stirring into about ten times its volume of cold water. The product separated as a gum which gradually hardened. When cold the solid was removed and the lumps crushed and washed several times with cold water. The crude product, light tan in color, weighed 8.4 g. (90%) and melted at 128–130°. Recrystallization from ethanol, with added Norit, gave colorless needles, m.p. 130–131°.

Anal. Calcd. for $C_{14}H_8O_2Cl_2$: C, 60.24; H, 2.89; Cl, 25.41. Found: C, 59.90; H, 2.80; Cl, 25.54.

3-(2,5-Dibromophenyl)phthalide. Five grams (0.033 mole) phthalaldehydic acid was dissolved in 45 ml. of 2:1 conc. sulfuric acid-20% fuming sulfuric acid. To this solution was added 7.86 g. (0.033 mole) of *p*-dibromobenzene, and the reaction vessel was then placed in an oil-bath at a bath temperature of 90–95° in order to maintain the insoluble *p*-dibromobenzene in a melted state for better dispersion. Following essentially the same procedure used in the preparation of 3-(2,5-dichlorophenyl)phthalide, there was obtained 12.2 g. (99%) of crude product, light ivory in color, m.p. 121–124°. Crystallization from ethanol, with added Norit, afforded colorless crystals, m.p. 124–125°.

Anal. Calcd. for $C_{14}H_8O_2Br_2$: C, 45.69; H, 2.19; Br, 43.43. Found: C, 45.49; H, 2.37; Br, 43.59.

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(14) E. D. Bergmann and E. Loewenthal, *Bull. soc. chim. France*, **1952**, 66–72.

Dicyclopropylglycolic Acid

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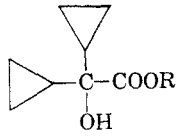
The interesting physiological activity of certain basic esters of benzilic acid is well known.[1] The availability of dicyclopropyl ketone through the convenient procedure of Hart and Curtis[2] has now made possible the preparation of the analog of benzilic acid, dicyclopropylglycolic acid (I).



I. R = H
II. R = CH_3
III. R = $—CH_2CH_2N(C_2H_5)_2 \cdot HCl$

Although Hart and Curtis showed that dicyclopropyl ketone reacts with the usual carbonyl reagents, we have been unable to prepare its cyanohydrin. Nor does it appear to form a chloroform addition product[3] from which the hydroxyacid could be derived. In these respects dicyclopropyl ketone resembles benzophenone.

The desired acid I was finally secured through permanganate oxidation of 1,1-dicyclopropyl-2-propyn-1-ol, derived from dicyclopropyl ketone by addition of sodium acetylide.[4] The yield of the oxidation step was only fair (40–45%).

Direct acid-catalyzed esterification of I could not be accomplished. Use of an ion exchange resin as the acid catalyst was no better. Likewise the action of either methyl iodide or dimethyl sulfate on the sodium salt of I produced no ester. Finally, however, II was obtained in 71% yield using diazomethane. The basic ester III was formed by treating the acid I with diethylaminoethyl chloride in isopropanol according to the method of Horenstein and Pählicke.[5]

EXPERIMENTAL

Dicyclopropylglycolic acid (I). To a stirred suspension of 40.8 g. (0.3 mole) of 1,1-dicyclopropyl-2-propyn-1-ol in 800 ml. of water held at 3–5° by means of an ice bath was added dropwise, over a period of 2.5 hr., a solution of 118.5 g. (0.75 mole) of potassium permanganate in 850 ml. of water. After stirring in the ice bath for another 1.5 hr., a large quantity of a filter aid (filtercel) was added and stirring was continued overnight in a refrigerated room.

The manganese dioxide and filter aid were collected at the filter and washed well with water. The combined filtrate and washings were decolorized with charcoal and extracted with ether from which, after drying and removal of ether by distillation, 6.0 g. (15%) of the acetylenic carbinol was recovered.

The ice-cold alkaline solution was acidified by the dropwise addition of cold concentrated sulfuric acid, and then extracted with five 200-ml. portions of ether. The combined ether extracts were dried over anhydrous magnesium sulfate. Filtration and removal of the ether by distillation gave

(1) Alfred Burger, *Medicinal Chemistry*, Interscience Publishers, Inc., New York, 1951, Vol. I, p. 423.
(2) H. Hart and O. Curtis, Jr., *J. Am. Chem. Soc.*, **78**, 112 (1956).
(3) C. Weizmann, E. Bergmann, and M. Sulzbacher, *J. Am. Chem. Soc.*, **70**, 1153, 1189 (1948).
(4) F. E. Fischer and K. E. Hamlin, in press.
(5) H. Horenstein and H. Pählicke, *Ber.*, **71**, 1644 (1938).

an oily semisolid product (33 g.) which was collected at the vacuum filter. Recrystallization from hexane (Skellysolve B) gave 12.3 g. of first crop, m.p. 83–85° and 6.1 g. of second, m.p. 82–84° (18.4 g. = 46% of theory, based on unrecovered carbinol). Several more recrystallizations for analysis raised the melting point to 84–86°.

Anal. Calcd. for $C_8H_{12}O_3$: C, 61.52; H, 7.75; O, 30.73. Found: C, 61.68; H, 7.97; O, 30.80.

The infrared spectrum was consistent with the assigned structure.

Methyl dicyclopropylglycolate (II). To a solution of 6 g. of diazomethane in 100 ml. of ether was added a solution of 8 g. (0.051 mole) of dicyclopropylglycolic acid (I) in 50 ml. of ether. After standing at room temperature in the dark for 24 hr., the ether was removed by distillation and the residual oil was distilled under reduced pressure. After a forerun, 2.1 g., b.p. 30–124° (60 mm.), the methyl ester II distilled at 124° (60 mm.); yield, 6.2 g. (71%), n_D^{23} 1.4535.

Anal. Calcd. for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.18; H, 8.51.

The infrared spectrum, including a band at 1.63 μ in the near infrared, characteristic of the cyclopropane ring,[6] was consistent with the assigned structure.

β-Diethylaminoethyl dicyclopropyglycolate hydrochloride (III). A solution of 7.8 g. (0.05 mole) of dicyclopropylglycolic acid (I) and 7.5 g. (0.055 mole) of β-diethylaminoethyl chloride in 60 ml. of isopropanol was refluxed with stirring for 18 hr. On cooling, the product crystallized. It was collected by vacuum filtration and dissolved in 50 ml. of cold water. Addition of excess cold 40% sodium hydroxide solution precipitated an oil (free ester base) which was taken up in ether, washed with water and dried over anhydrous sodium sulfate. After removal of the drying agent by filtration, a slight excess of ethereal hydrogen chloride solution was added and the precipitated hydrochloride was collected. Three recrystallizations from ethanol gave 6.5 g. (45%) of the ester hydrochloride III, m.p. 152–154°.

Anal. Calcd. for $C_{14}H_{26}ClNO_3$: C, 57.62; H, 8.98; N, 4.80; Cl, 12.15. Found: C, 57.77; H, 8.98; N, 4.82; Cl, 12.17.

(6) W. H. Washburn and M. J. Mahoney, *J. Am. Chem. Soc.*, **80**, 504 (1958).

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Synthesis of 3-Hydroxypyridines. I. Condensation of Aromatic Aldehydes with Ethyl Cyanoacetate

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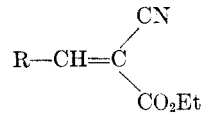
In the course of investigations of methods of syntheses of 3-hydroxypyridines in progress in this laboratory, it was necessary to prepare a series of compounds of type I.



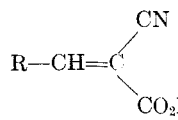
The α,β-unsaturated cyanoesters, I, in which R is an aromatic group, were prepared by condensation of the appropriate aromatic aldehyde with ethyl cyanoacetate by the general Knoevenagel[1] reaction using piperidine as a catalyst.[2] In this

(1) J. Scheiber and F. Meisel, *Ber.*, **48**, 257 (1915).

(2) See for example P. D. Gardner and R. I. Brandon, *J. Org. Chem.*, **22**, 1704 (1957).

TABLE I

CONDENSATION OF ALDEHYDES WITH ETHYL CYANOACETATE



R	Yield, %	M.P.[a]	Calcd. Carbon	Calcd. Hydrogen	Calcd. Nitrogen	Found[b] Carbon	Found[b] Hydrogen	Found[b] Nitrogen
o-ClC_6H_4—	61	54–55[c,d]	61.16	4.28	5.95	61.11	4.03	5.97
3,4-$(C_2H_5O)_2C_6H_3$—	86	126–127[c]	66.42	6.62	4.84	66.40	6.64	4.95
p-$(ClCH_2CH_2)_2NC_6H_4$—	89	174–175[e]	56.31	5.32	8.21	56.38	5.54	7.93
3,4-$(CH_2O_2)C_6H_3$—	77	106–107[c,f]	63.67	4.52	5.71	63.70	4.63	5.47
o-$O_2NC_6H_4$—	68	101–103[c,g]	58.53	4.09	11.38	58.82	4.16	11.60
3-CH_3O-4-HOC_6H_3—	92	108–109[c,h]	63.15	5.30	5.67	63.13	5.39	5.90
p-HOC_6H_4—	58	173–174[c,i]	66.35	5.11	6.45	66.69	5.05	6.23
p-$(CH_3CH_2)_2NC_6H_4$—	81	95–96[c]	70.56	7.40	10.29	70.42	7.49	10.09
o-$O_2NC_6H_4CH{=}CH$—	83	141–142[c]	61.76	4.44	10.29	62.21	4.42	10.42

[a] All melting points are uncorrected. [b] Analyses by Spang Microanalytical Laboratory, Ann Arbor, Mich., and Drs. Weiler and Straus, Oxford, Eng. [c] Recrystallized from 95% ethanol. [d] Reported m.p. 53° (from esterification of acid), J. A. McRae and C. Y. Hopkins, *Can. J. Res.*, **7**, 248 (1932). [e] Recrystallized from chloroform. [f] Reported m.p. 104° (from esterification of acid), C. H. Clarke and F. Francis, *Ber.*, **44**, 273 (1911). [g] Reported m.p. 96° (from condensation reaction), F. Reidel, *J. prakt. Chem.*, (2), **54**, 533 (1896). [h] Reported m.p. 111° (from esterification of acid), reference as footnote f. [i] Reported m.p. 162–163° (from condensation reaction), reference as footnote g.