TABLE I

General name	Alkoxy groups	Yield, %	B.p., °C.[a] or crystn. solv. °C.	Mm.	M.p.,[b] °C.	Molecular formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
2,5-Dialkoxyacetophenone	CH_3O	68	116	2	21[c,d]	$C_{10}H_{12}O_3$				
	C_2H_5O	52	129	3	41[e]	$C_{12}H_{16}O_3$				
	n-C_3H_7O[f]	63	138	2	19[c]	$C_{14}H_{20}O_3$	71.1	70.8	8.53	8.67
	n-C_4H_9O[g]	72	152	2	26[c]	$C_{16}H_{24}O_3$	72.7	72.6	9.15	9.08
2,5-Dialkoxyphenylacetic acid	CH_3O	64	Water		123[h]	$C_{10}H_{12}O_4$				
	C_2H_5O	37	37% EtOH		89	$C_{12}H_{16}O_4$	64.3	64.3	7.22	7.25
	n-C_3H_7O	63	Pet.[i]		66	$C_{14}H_{20}O_4$	66.6	66.3	7.99	8.17
	n-C_4H_9O	29	30% EtOH		53	$C_{16}H_{24}O_4$	68.6	68.5	8.63	8.44
2,5-Dialkoxyphenylacetamide	CH_3O	82	Water		133	$C_{10}H_{13}O_3N$	31.8[j]	32.1[j]	7.18[k]	7.01[k]
	C_2H_5O	70	Water		111	$C_{12}H_{17}O_3N$			6.28[k]	6.19[k]
	n-C_3H_7O	88	C_6H_6–Pet.[i]		115	$C_{14}H_{21}O_3N$			5.57[k]	5.55[k]
	n-C_4H_9O	86	C_6H_6–Pet.[i]		88	$C_{16}H_{25}O_3N$			5.02[k]	4.99[k]
Methyl 2,5-dialkoxyphenylacetate	CH_3O	93	128	3	44[l]	$C_{11}H_{14}O_4$				
	C_2H_5O	69	127	2	[m]	$C_{13}H_{18}O_4$	65.5	65.0	7.60	7.54
	n-C_3H_7O	84	134	2	[m]	$C_{15}H_{22}O_4$	67.6	67.3	8.32	8.49
	n-C_4H_9O[n]	50	178	3	18[c]	$C_{17}H_{26}O_4$	69.4	69.2	8.90	9.24

[a] Uncorrected; lower limit of 2 degree range listed. [b] Taken in apparatus calibrated with standard compounds. [c] Freezing point. [d] Lit.: 20–22° (ref. 4). [e] Lit.: 42° (ref. 4.) [f] 2,4-Dinitrophenylhydrazone, m.p. 107°. *Anal.* Calcd. for $C_{20}H_{24}O_6N_4$: N, 13.45. Found: N, 13.68. [g] 2,4-Dinitrophenylhydrazone, m.p. 116°. *Anal.* Calcd. for $C_{22}H_{28}O_6N_4$: N, 12.61. Found: N, 12.61. [h] Lit.: 123–124° (ref. 2). [i] Pet. ether, b.p. 60–90°. [j] Methoxyl. [k] Nitrogen %. [l] Lit.: 45° (ref. 5). [m] Did not solidify after 4 hr. in Dry Ice-bath. [n] $n^{25}D$ 1.4954.

TABLE II

Alkoxy groups	T, °C.	n^tD	d^t_4	Molar refraction Found[a]	Molar refraction Calcd.[6]
2,5-Dialkoxyacetophenones					
CH_3O	20	1.5430	1.1401[b]	49.82	48.77[c]
n-C_3H_7O	25	1.5150	1.0368	68.72	67.24[c]
n-C_4H_9O	30	1.5067	1.0076	78.07	76.47[c]
Methyl 2,5-dialkoxyphenylacetates					
C_2H_5O	25	1.5070	1.0997	64.38	63.57
n-C_3H_7O	25	1.4991	1.0564	74.05	72.81

[a] From Lorentz–Lorenz equation. [b] Lit.: 1.1385 (ref. 4). [c] Includes exaltation of 0.69 for conjugation of carbonyl and aromatic double bonds.

The yields, physical constants and analyses are listed in Tables I and II.

2,5-Dialkoxyphenylacetic Acids.—The general method of Abbott and Smith[2] for the preparation of 2,5-dimethoxyphenylacetic acid from 2,5-dimethoxyacetophenone by the Willgerodt reaction was used. In the case of the di-*n*-propoxy- and di-*n*-butoxy-compounds, acidification of the basic hydrolysis solution yielded a dark oil which was dissolved in ether and extracted repeatedly with potassium bicarbonate solution followed by acidification of the aqueous extracts. The yields, physical constants, analyses and crystallization solvents are listed in Table I.

2,5-Dialkoxyphenylacetamides.—One-tenth of a mole of the 2,5-dialkoxyphenylacetic acid and 22 ml. of thionyl chloride were refluxed for 30 minutes. The resulting solution was poured slowly into 100 ml. of ice-cold concentrated ammonium hydroxide. The crude product was filtered off and recrystallized. The yields, physical constants, analyses and crystallization solvents are listed in Table I.

Methyl 2,5-Dialkoxyphenylacetates.—One-tenth of a mole of the 2,5-dialkoxyphenylacetic acid and 22 ml. of thionyl chloride were refluxed for 30 minutes. Then 150 ml. of absolute methanol were added dropwise with cooling. After addition was complete, the reaction mixture was allowed to stand at room temperature for 30 minutes and then refluxed for 30 minutes. Excess volatile reagents and by-products were removed by evaporation, and the residual oil was fractionated twice through a 15-cm. Vigreux column.

The yields, physical constants and analyses are listed in Tables I and II.

2,5-Dihydroxyphenylacetic Acid.—This compound was prepared in a yield of 76% by the demethylation of 2,5-dimethoxyphenylacetic acid[2] and in yields of 38–47% by the condensation of *p*-quinone with ketene diethylacetal followed by hydrolysis.[3]

Acknowledgments.—The authors are indebted to The Wm. S. Merrell Co., Cincinnati, Ohio, for a grant in support of this work and for the pharmacological testing of some of the compounds synthesized, and to the Tennessee Eastman Corporation, Kingsport, Tennessee, for a generous supply of the 1,4-dialkoxybenzenes used as starting materials.

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RECEIVED JULY 23, 1951

The Preparation of Di- and Triphenylacetonitrile and Their Cuprous Halide Complexes

BY WALTER M. BUDDE AND SYLVESTER J. POTEMPA

Although a good preparation for diphenylacetonitrile (II) has been described[1] it was decided to attempt a method which would involve fewer time-consuming steps and no lachrymatory intermediates. The process developed was the reaction of benzhydryl bromide (I) with anhydrous cuprous cyanide.

$$\underset{\text{I}}{(C_6H_5)_2CHBr} + CuCN \longrightarrow \underset{\text{II}}{(C_6H_5)_2CHCN} + CuBr$$

I was prepared in 70–75% yield by the action of phosphorus tribromide on benzhydrol. Heating I with a slight molar excess of oven-dried cuprous cyanide at 125° produced pure II in 75–80% yield after distillation. It was noticed that if impure I was used there was a pronounced tendency to form a stable complex molecule, III, dec. pt. 155°.

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(4) I. M. Heilbron and H. M. Bunbury, "Dictionary of Organic Compounds," Vol. III, Oxford University Press, New York, N. Y., 1938, p. 568.

(5) *Ibid.*, Vol. II, p. 194.

(6) H. Gilman, "Organic Chemistry," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1943, p. 1751.

(1) C. Robb and E. Schultz, *Org. Syntheses*, **28**, 55 (1948).

$$(C_6H_5)_2CHC{\equiv}N \longrightarrow CuBr$$

III

The chief impurities present in impure I were presumably benzhydrol and dibenzhydryl ether. Compounds of the type III have been previously reported[2] but the ones investigated heretofore were somewhat less stable. Attempts in this Laboratory to synthesize III by other methods were unsuccessful. The methods tried were heating II with freshly prepared cuprous bromide, heating II with a mixture of cupric bromide and activated copper powder, and heating a mixture of II, cupric bromide, and activated copper powder with acetonitrile as a solvent.

The structure of III was fairly well established by two means: (1) analytical data checked very closely with calculated values; (2) vacuum distillation of pure III produced practically theoretical amounts of II in the distillate and cuprous bromide in the residue. The possibility that III was a complex of the isonitrile type (IV) was rejected for three reasons: (1) Compounds of the type IV

$$(C_6H_5)_2CH{-}N{=}C \longrightarrow CuBr$$

IV

have been prepared[3] and all are described as being deeply colored, while III is colorless; (2) vacuum distillation was not considered sufficient to convert the isonitrile into the nitrile form. In other instances of these transitions longer heating was required[4]; (3) heating III above its decomposition point did not produce, even momentarily, a characteristic isonitrile odor.

Attempts to substitute benzhydryl chloride for I were abandoned because poor yields of II were produced each time (40–50%). A high-melting nitrogen-containing organic compound was isolated as a by-product but was not further identified. Even with pure benzhydryl chloride the corresponding complex molecule $(C_6H_5)_2CHCN \rightarrow CuCl$ was formed in considerable proportion. It was isolated as a light tan crystalline solid, dec. pt. 119–121°.

Heating purified trityl chloride with dry cuprous cyanide at 125° affords triphenylacetonitrile,[5] (V) in 65–70% yield. When impure trityl chloride was employed the chief product was the corresponding complex molecule VI. This compound is

$$(C_6H_5)_3C{-}CN \longrightarrow CuCl$$

VI

colorless when pure, but assumes a purplish color when allowed to stand in air. Qualitative analysis showed the expected elements to be present; distillation of the dry material produced the theoretical amounts of residual cuprous chloride and distilled triphenylacetonitrile. In this case it was established that the chief impurity present in the trityl chloride was triphenylcarbinol.

Experimental

All melting and decomposition points are corrected.

Benzhydryl bromide (I) b.p. 150–155°, 2 mm., m.p. 46° was prepared by a modification of the method of Claisen.[6]

Diphenylacetonitrile (II).—In a flask subsequently used for a vacuum distillation, was placed pure I (35.2 g., 0.143 mole) which was heated with stirring to 125° in an oil-bath. Cuprous cyanide (14.1 g., 0.157 mole) (J. T. Baker Chemical Co.), dried at 110° for two hours, was then added all at once. The mixture quickly darkened, and a heavy precipitate of cuprous bromide began to separate. The stirring and heating were continued for 45 minutes, and then a vacuum stillhead and receiver were attached to the reaction flask, and the entire mixture vacuum distilled. Precautions were taken to avoid bumping, and solidification of the product in the delivery tube. The colorless oil which distilled solidified in the receiver. This solid melted at 74–75°, and amounted to 20.6 g. (75%) (b.p. 158° at 4 mm.). Recrystallization from isopropyl alcohol gave a product melting at 74.5–75°. When larger amounts of the starting materials were used the percentage yields were a little higher (75–78%).

Formation of Diphenylacetonitrile–Cuprous Bromide Complex (III).—The greatest tendency for this product to form was noted when, in the preparation of I, petroleum ether was used in place of ether as an extraction solvent, and the benzhydryl bromide was not vacuum distilled. When molar quantities of undistilled I and cuprous cyanide were used as described in the above experiment, it was observed that after about one-half hour of heating at 125° the whole mass solidified and stopped the stirrer. The solid mixture was cooled, ground to a powder and extracted for five hours with benzene in a soxhlet extractor. Evaporation of the benzene gave 7.0 g. of impure II. The benzene-insoluble residue was further extracted with chloroform for six hours. The hot chloroform deposited 21.1 g. of the complex III in the form of hard, gleaming white prisms. The residue in the soxhlet cup consisted almost entirely of cuprous bromide and excess cuprous cyanide. In the several runs of this sort that were made the ratio of complexed to uncomplexed II was variable, ranging from about 4:1 to 2:1 by weight.

Anal. Calcd. for $C_{14}H_{11}BrNCu$: C, 49.94; H, 3.29; Br, 23.74; N, 4.16; mol. wt., 336.73. Found: C, 49.98; H, 3.24; Br, 23.64; N, 4.16; mol. wt. (ebulliometrically in chloroform), 288.

Triphenylacetonitrile (V).—Purified trityl chloride (Eastman Kodak Co. product) m.p. 110° (15.8 g., 0.057 mole) was heated to 125° with mechanical stirring, and oven-dried cuprous cyanide (6.6 g., 0.0623 mole) was added. The mixture was heated and stirred for 1.5 hours, and it thickened slightly during this time. The cooled solid mixture was extracted with 100 ml. of boiling benzene, followed by two 30-ml. portions. The solid residue remaining weighed 5.94 g., which amounted to 98.5% of the theoretical amounts of cuprous chloride and excess cuprous cyanide. Upon evaporation of the filtered benzene extracts there remained 14.4 g. (94%) of impure triphenylacetonitrile, m.p. 101–104°. One recrystallization of this brown solid from isopropyl alcohol using decolorizing charcoal gave 9.5 g. (62%) of a white product which melted at 124–125°. The reported melting point[5] is 127.5°.

Formation of Triphenylacetonitrile–Cuprous Chloride Complex (VI).—When the above directions were followed using an old unpurified sample of commercial trityl chloride (m.p. 95–109°), the cooled benzene extract deposited 8.5 g. of a white solid. This material turned purple when exposed to the air. It was decomposed by dry distillation to give almost the theoretical amounts of triphenylacetonitrile in the distillate and cuprous chloride in the residue. The decomposition point of the complex was distinct, but above 190°. Qualitative analysis showed Cu, Cl and N to be present. The benzene extracts from which VI had been removed were evaporated. The residue consisted of triphenylacetonitrile, m.p. 101–105°.

Reaction of Benzhydryl Chloride with Cuprous Cyanide.—Benzhydryl chloride was prepared in 61% yield by a method analogous to that used for benzhydryl bromide. It distilled at 134–135° at 2 mm. A voluminous unidentified solid residue was left in the distillation flask. When benzhydryl chloride reacted with cuprous cyanide in the same manner as benzhydryl bromide (see above) the mixture partially solidified after one-half hour of heating. There could be isolated from the reaction mixture the complex of diphenyl-

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[2] H. Morgan, *J. Chem. Soc.*, 2901 (1923).

[3] I. Malatesta, *Gazz. chim. ital.*, **77**, 240 (1947).

[4] N. Sidgwick, "The Organic Chemistry of Nitrogen," Oxford Press, London, 1937, p. 318.

[5] E. Fischer and O. Fischer, *Ann.*, **194**, 261 (1878).

[6] L. Claisen, *Ann.*, **442**, 245 (1925).

acetonitrile and cuprous chloride by extraction with hot benzene, from which it crystallized on cooling.

Anal. Calcd. for $C_{13}H_{11}ClNCu$: C, 57.53; H, 3.79. Found: C, 57.34; H, 3.48.

Evaporation of the cooled benzene extracts afforded a 40–50% yield of II, admixed with the unidentified compound described below. If the original reaction mixture was distilled before extraction with benzene, there remained in the undistilled residue an organic compound of high melting point which contained nitrogen. In a run using the same amounts of starting materials as described for benzhydryl bromide, about 4–5 g. of this benzene-soluble compound was formed. Its identification was not undertaken.

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Synthesis of Diphenylalkylcyclopentanones

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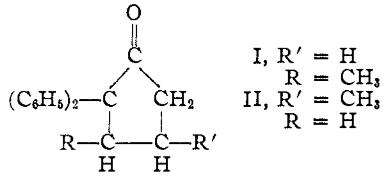
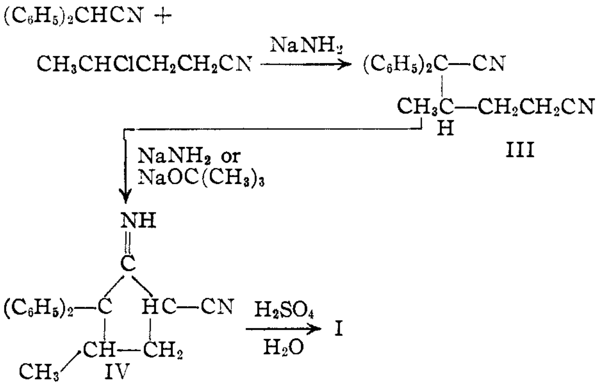
No preparation of diphenylalkylcyclopentanones has been reported in the literature and due to their similarity to a deaminated, cyclized Methadone it seemed advisable to investigate the synthesis of compounds of this type.



I, R′ = H
R = CH_3
II, R′ = CH_3
R = H

Two examples—2,2-diphenyl-3-methylcyclopentanone (I) and 2,2-diphenyl-4-methylcyclopentanone (II) were selected. The synthesis of I is shown in the following scheme.



Reaction of 1-iodo-3-chlorobutane with one mole of sodium cyanide converted this compound to γ-chlorovaleronitrile, which was condensed with diphenylacetonitrile in the presence of sodamide to give III. However, considerable cyclization to IV occurred during this reaction. The linear compound III could then be cyclized with sodamide or in a better yield using sodium tertiary butoxide as the catalyst. The hydrolysis and decarboxylation of IV gave I.

The ketone II was prepared in a similar manner using γ-chloroisovaleronitrile.

γ-Chloroisovaleronitrile (V) was prepared from γ-chloroisobutyl bromide by treatment with an equivalent of sodium cyanide.

Experimental

The 1,3-dichlorobutane was prepared according to Clarke and Streight.[1] The 1-iodo-3-chlorobutane was prepared according to Hass and Huffman.[2]

Preparation of γ-Chlorovaleronitrile.—Into a three-neck one-liter flask equipped with a dropping funnel, a mechanical stirrer, and a gas trapped reflux condenser was placed 10.1 g. (0.206 mole) of sodium cyanide and 60 cc. of water. After solution of the sodium cyanide 200 cc. of 95% ethyl alcohol was added, followed by 37.5 g. (0.172 mole) of 1-iodo-3-chlorobutane. The mixture was refluxed for six hours and then cooled. The cooled solution was diluted with 225 cc. of water and the solution was then extracted with three 50-cc. portions of chloroform. The chloroform layers were separated and washed twice with an equal volume of half-saturated calcium chloride solution, and then washed twice with an equal volume of water. The organic layer was dried over calcium chloride and stored in the refrigerator in a container covered with aluminum foil to prevent decomposition. The solution was filtered and the filtrate subjected to a distillation to remove the chloroform. The residue was then distilled under reduced pressure and 14.6 g. (72.3% yield) of a clear colorless liquid with a boiling range of 95–110° at 40–44 mm. pressure was collected. Gresham[3] found the boiling point to be 55° at 2 mm.

Condensation of γ-Chlorovaleronitrile and Diphenylacetonitrile in the Presence of Sodamide.—Into a three-neck 500-cc. flask equipped with a dropping funnel, a mechanical stirrer, and a reflux condenser with attached calcium chloride drying tube was placed 250 cc. of dry benzene followed by 5.3 g. (0.136 mole) of sodamide. To this mixture was added with stirring, 25 g. (0.129 mole) of diphenylacetonitrile. The mixture was refluxed for three hours, during which time evolution of ammonia occurred (during this period the drying tube was removed for the condenser), and then cooled to room temperature. To the resulting mixture was added dropwise 14.6 g. (0.124 mole) of γ-chlorovaleronitrile. The mixture was refluxed for four hours, cooled and then poured into 300 cc. of water. The layers were separated, the benzene layer washed three times with an equal volume of water and then dried over anhydrous magnesium sulfate. After filtration of the magnesium sulfate, the benzene was removed from the solution by distillation. The resulting oil was placed in the refrigerator. Within 48 hours, partial crystallization had occurred. The oil was filtered and the crystalline solid was carefully washed with ether. Approximately 1.5 g. of a solid was obtained which, when recrystallized from methanol, yielded white crystals melting at 164–166°.

The balance of the oil and the ethereal washings when concentrated and then subjected to a series of fractional distillations at one mm. pressure, yielded 8.5 g. of diphenylacetonitrile from the fraction distilling at 0–150° and 1.5 g. of the cyclic ketimine from the fraction distilling at 150–210°. The total yield of 2,2-diphenyl-3-methyl-5-cyanocyclopentanone imine was 3 g. (8.8% yield).

Anal. Calcd. for $C_{19}H_{18}N_2$: N, 10.22. Found: N, 10.10.

Preparation of 2,2-Diphenyl-3-methylcyclopentanone.—Into a one-neck 200-cc. flask equipped with a reflux condenser was placed 1.4 g. (0.00511 mole) of finely divided 2,2-diphenyl-3-methyl-5-cyanocyclopentanone imine and a cold sulfuric acid solution made up of 1.5 cc. of water and 5 cc. of concentrated sulfuric acid. After the addition was complete, the flask was heated on a water-bath until solution occurred and then for 15 minutes longer. The solution was cooled and 25 cc. of water added. The mixture was then heated to reflux, at which time 30 cc. of glacial acetic acid was added to increase the miscibility of the two layers present, and the solution was refluxed for 25 hours. The reaction mixture was then cooled, diluted with 200 cc. of water, and extracted with three 40-cc. portions of ether. The ether layers were combined and washed with several portions of 5% sodium hydroxide solution, and dried over anhydrous magnesium sulfate. The solution was filtered and the filtrate concentrated under reduced pressure until the volume was reduced to 5–8 cc. (at this point some nearly white solid had formed) and was then stored in the

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[1] R. H. Clarke and H. R. L. Streight, *Trans. Roy. Soc. Can. Series* 3, Vol. 23, Sec. III (77) 1929.

[2] H. B. Hass and H. C. Huffman, THIS JOURNAL, **63**, 1233 (1941).

[3] Wm. F. Gresham, U. S. Patent 2,405,948.