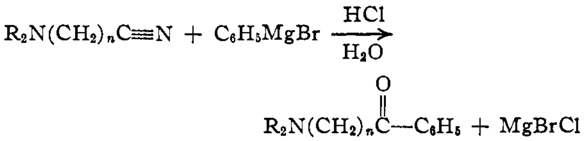
of 14.83% chloride. This does not correspond to the hydrochloride derivative of the expected ketone, γ-piperidinobutyrophenone (13.24%), or to the dihydrochloride of the ketimine (23.38%). However, the free basic ketone could be obtained by treating this solid with 6 *N* sodium hydroxide in the presence of ether. The hydrochloride derivative prepared from the purified base melts at 180°. A similar phenomenon was also noted in the preparation of higher homologs.

By the preparation of δ-piperidinovalerophenone, and ε-piperidinocaprophenone, it is now evident that the reaction



$$R_2N(CH_2)_nC{\equiv}N + C_6H_5MgBr \xrightarrow[H_2O]{HCl} R_2N(CH_2)_n\overset{\overset{\displaystyle O}{\|}}{C}{-}C_6H_5 + MgBrCl$$

is general when "*n*" is equal to or more than three. It has already been shown by Bruylants[8] that anomalous reactions may occur when "*n*" is one. We have attempted several reactions when "*n*" is two, but only polymers were isolated confirming the previous report of Bruylants.[9]

Experimental

γ-Diethylaminobutyronitrile.—This was made as previously described[5] with the exception that 0.05 mole per cent. of sodium iodide was added as catalyst. This facilitated the reaction and raised the yield to 88.1%. When γ-bromobutyronitrile[10] was refluxed with excess diethylamine under these same conditions a 96.7% yield of γ-diethylaminobutyronitrile was obtained.

δ-Piperidinovaleronitrile.—This was prepared from δ-chlorovaleronitrile[11] and piperidine as described for the next lower homolog[5] and had the following properties: b. p. 107° (3 mm.), n^{20}D 1.4659, hydrochloride derivative m. p. 150–151°.

ε-Piperidinocapronitrile.—This was prepared from ε-bromocapronitrile[12] in an analogous manner: b. p. 122° (3 mm.), n^{20}D 1.4666, hydrochloride derivative m. p. 124°.

Preparation of γ-Piperidinobutyrophenone.—To 12 g. (0.5 mole) of magnesium turnings, 50 ml. of dry ether, and a small crystal of iodine, was slowly added 85 g. (0.54 mole) of bromobenzene dissolved in 100 ml. of ether. To the reagent thus prepared was added 38.0 g. (0.25 mole) of γ-piperidinobutyronitrile[6] dissolved in an equal volume of ether, and the reaction mixture was allowed to stand overnight. The reaction was hydrolyzed by pouring onto a mixture of 400 ml. of 6 *N* hydrochloric acid and 200 g. of ice. The white precipitate formed was filtered and treated with 6 *N* sodium hydroxide in the presence of ether. Distillation of the residue from the ether extract through a Claisen flask gave 21.0 g. of γ-piperidinobutyrophenone, b. p. 144–146° at 3 mm., n^{20}D 1.5348, in 64.1% yield. A Volhard chloride determination on the hydrochloride derivative (m. p. 180°) showed 13.12% chlorine; calculated 13.24%.

Preparation of δ-Piperidinovalerophenone.—In an identical manner, δ-piperidinovalerophenone was prepared in 50% yield; b. p. 167° at 3 mm., n^{25}D 1.5289. An equivalent weight determination obtained by titration with hydrochloric acid using methyl orange indicator gave a value of 245.1; calculated, 245.2. A Volhard chloride determination on the hydrochloride derivative (m. p. 170–172°) showed 12.49% chloride; calculated, 12.59%.

Preparation of ε-Piperidinocaprophenone.—Acid hydrolysis of the reaction mixture in this case gave only small quantities of a white crystalline precipitate. The solution was made strongly basic, extracted with three portions of ether, and the extracts distilled to give ε-piperidinocaprophenone (b. p. 158–160° at 0.4 mm., n^{20}D 1.5280) in 55.6% yield. A satisfactory equivalent weight could not be obtained upon titration with acid, however, a Volhard chloride determination on the hydrochloride (m. p. 146–148°) gave a value of 12.02% chlorine; calculated, 11.98%.

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[8] Bruylants, *et al.*, *Bull. sci. acad. roy. Belg.*, **10**, 126 (1924): **11**, 261, 301 (1925); *Bull. sci. chim. Belg.*, **33**, 467 (1924): **33**, 483 (1924).

[9] Bruylants, *Bull. soc. chim. Belg.*, **32**, 266 (1923).

[10] Obtained by carefully fractionating the reaction product from trimethylene chlorobromide and potassium cyanide (Allen, *Organic Syntheses*, Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 156).

[11] Starr and Hixon, THIS JOURNAL, **56**, 1595 (1934).

[12] Trunel, *Compt. rend.*, **197**, 453 (1933).

The Synthesis of Bis-(dialkylaminoalkyl) Esters of 5-Methoxyisophthalic Acid[1,2]

BY J. C. CALANDRA AND J. J. SVARZ

It has been found that basic-alkyl esters of 4-methoxy-[3] and 4-fluoroisophthalic acid[4] exhibit local anesthetic activity. This work is a continuation of earlier studies and deals with the synthesis of the basic-alkyl esters of 5-methoxyisophthalic acid. The results of the pharmacological studies will be presented elsewhere.

Experimental

5-Methoxy-1,3-dimethylbenzene.—A commercial sample of 5-hydroxy-1,3-dimethylbenzene was purified by fractional distillation and the methyl ether was prepared according to the method of Ullmann.[5] The yield was 88%; b. p. 113–114° (50 mm.) and 192–194° at atmospheric pressure; d^{25}_{25} 0.9580, n^{25}D 1.5105.

5-Methoxyisophthalic Acid.—This compound was prepared using the method described by Fosdick and Fancher.[3] The acid was obtained as a white solid in a 54.3% yield, m. p. 267–268°. *Neut. equiv.* Calcd. for $C_9H_8O_5$: 98.03. Found: 98.50.

5-Methoxyisophthalyl Chloride.[3]—This compound was obtained in 75.5% yield, m. p. 48–49°. *Anal.* Calcd. for $C_9H_6O_3Cl_2$: Cl, 30.12. Found: Cl, 29.97.

Dimethyl 5-Ethoxyisophthalate.[3]—This compound recrystallized from methanol was prepared in 92% yield, m. p. 110.5–111°. *Anal.* Calcd. for $C_{11}H_{12}O_5$: C, 58.92; H, 5.40. Found: C, 58.94; H, 5.41.

Bis-(dialkylaminoalkyl)-5-methoxyisophthalate Di-hydrochloride.—These esters were prepared using the method mentioned above[3] with a slight modification in that two moles of the aminoalkanols were treated with one mole of the acid chloride in the absence of a solvent. All of these compounds possess local anesthetic activity. The analytical data are presented in Table I.

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[1] Presented before the Division of Medicinal Chemistry at the 110th meeting of the American Chemical Society at Chicago, Illinois, September 12, 1946.

[2] From the Master of Science thesis of J. J. Svarz.

[3] L. S. Fosdick and O. E. Fancher, THIS JOURNAL, **63**, 1277 (1941).

[4] L. S. Fosdick and J. C. Calandra, *ibid.*, **65**, 2308 (1943).

[5] F. Ullmann, *Ann.*, **327**, 104 (1903).

TABLE I

BIS-DIALKYLAMINOALKYL 5-METHOXYISOPHTHALATE DIHYDROCHLORIDES

Bis-dialkylaminoalkyl 5-methoxyisophthalate dihydrochloride	Yield, %	M. p., °C.	Formula	Nitrogen, % Calcd.	Nitrogen, % Found
β-(Dimethylamino)-ethyl	46.0	224–225	$C_{17}H_{28}O_5N_2Cl_2$	6.81	6.71
β-(Diethylamino)-ethyl	59.5	227	$C_{21}H_{36}O_5N_2Cl_2$	5.99	6.07
γ-(Diethylamino)-propyl	72.5	178–179	$C_{23}H_{42}O_5N_2Cl_2$	5.65	5.64
β-(Di-n-propylamino)-ethyl	50.0	151–152	$C_{25}H_{44}O_5N_2Cl_2$	5.35	5.28
γ-(Di-*n*-propylamino)-propyl	65.8	139–140	$C_{27}H_{48}O_5N_2Cl_2$	5.07	4.94
β-(Di-isopropylamino)-ethyl	52.0	188–189	$C_{25}H_{44}O_5N_2Cl_2$	5.35	5.23
γ-(Di-isopropylamino)-propyl	63.8	119	$C_{27}H_{48}O_5N_2Cl_2$	5.07	5.00
β-(Di-*n*-butylamino)-ethyl	69.1	137.5–138.5	$C_{28}H_{52}O_5N_2Cl_2$	4.83	4.74
γ-(Di-*n*-butylamino)-propyl	63.5	127–128	$C_{31}H_{56}O_5N_2Cl_2$	4.59	4.50
β-(Di-*n*-amylamino)-ethyl-[a]	65.2	....	$C_{33}H_{58}O_5$	4.96	4.78
γ-(Di-*n*-amylamino)-propyl	35.8	70–72	$C_{35}H_{64}O_5N_2Cl_2$	4.22	4.22
β-(Di-*n*-hexylamino)-ethyl[b]	62.1	64–65	$C_{37}H_{66}O_5N_2Br_2$	3.59	3.63
γ-(Di-*n*-hexylamino)-propyl	77.5	75–76	$C_{39}H_{74}O_5N_2Cl_2$	3.89	3.96

[a] Free base b. p. 205–210° (0.05 mm.). [b] Dihydrobromide.

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[6] Original manuscript received July 16, 1947.

The Formation of Biphenyl in the Decomposition of Benzoyl Peroxide in Nitrobenzene

BY DELOS F. DETAR

In the decomposition of diacyl peroxides $(ArCOO)_2$ in aromatic solvents it has been observed[1] that the principal product is the unsymmetrical biaryl ArAr[1] formed by attack on the solvent. In the decomposition of benzoyl peroxide in nitrobenzene Wieland, Schapiro and Metzger[2] were unable to detect any of the symmetrical product, biphenyl. With the idea that more biphenyl might be formed in more concentrated solutions, the experiment[2] was repeated with 20–40% solutions. Biphenyl was definitely formed and probably in at least 3–4% yields since the isolation method is known to involve losses. The biphenyl may have been formed by either a coupling of two phenyl radicals, or by an induced decomposition of the peroxide by a phenyl radical.[3,4] No more than a trace of the symmetrical 4,4′-dinitrobiphenyl could have been present since none could be found. It is much less soluble than the 4-nitrobiphenyl and is detectable in mixtures with it.

Experimental

Decomposition of Benzoyl Peroxide in Nitrobenzene.—Benzoyl peroxide (5.00 g.) was added to 15 g. of nitrobenzene and the mixture warmed at 110° for one-half hour (homogeneous solution). The reaction mixture was steam distilled, the distillate extracted with alkali and then the nitrobenzene layer was reduced with tin and hydrochloric acid.[5] Steam distillation of the reduction mixture followed by extraction with peroxide-free ether gave a neutral residue. This was refluxed with 10% sodium hydroxide solution to assure removal of phenyl benzoate. The residue amounted to 44 mg. (1.4%). It was identified as biphenyl by microscopic comparison with authentic biphenyl by identity of the 70° angle of the rhombic-shaped plates obtained from ethanol and the extinction angles which bisected the vertices. Other runs at 90° and one decomposition of a 40% solution of benzoyl peroxide gave similar results.

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[1] *Cf.* Waters, "The Chemistry of Free Radicals," Oxford University Press, London, 1946, p. 165.

[2] Wieland, Schapiro and Metzger, *Ann.*, **513**, 105 (1934).

[3] Nozaki and Bartlett, THIS JOURNAL, **68**, 1686 (1946).

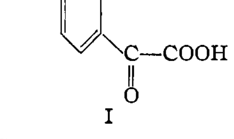
[4] DeTar and Sagmanli, *ibid.*, **72**, 965 (1950).

[5] This reduction method was used by Wieland, Schapiro and Metzger.[2]

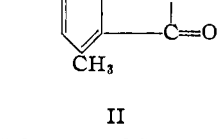
The Ultraviolet Absorption Spectra of Several Substituted Phenylglyoxylic Acids

BY DONALD J. CRAM

In connection with a study on the structure of citrinin, the compounds I,[1] II,[1] III[1] and IV[1] were synthesized as models for an ultraviolet absorption spectra comparison with citrinin. Although the recent resynthesis of this natural product[2] made such a study unfeasible, an examination of the spectra of these molecules reveals some interesting structural relationships.



I



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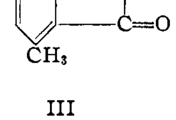
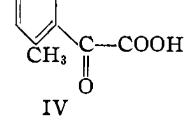


III



IV

Hunsberger, *et al.*,[1] reported that methylation of II with dry diazomethane produced a monomethylated compound that possessed the hemiquinone

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[1] Hunsberger and Amstutz, THIS JOURNAL, **70**, 671 (1948).

[2] Robertson, *et al.*, *Nature*, **163**, 94 (1949).