Similarly prepared were: **4-(Diethylaminoacetylamino)-2-butoxybenzoic acid hydrochloride**, m.p. 205.4–206° dec. *Anal.* Calcd. for $C_{17}H_{27}ClN_2O_4$: N, 7.81. Found: N, 7.65.

4-(Diethylaminoacetylamino)-2-benzyloxybenzoic acid hydrochloride, m.p. 180.7–182.0°. *Anal.* Calcd. for $C_{20}H_{25}ClN_2O_4$: N, 7.13; Cl, 9.02. Found: N, 7.34; Cl, 8.90.

2-Methoxy-4-nitrobenzamide.—To 1 liter of cooled, stirred, concentrated ammonium hydroxide (28%) there was added, portionwise, 70 g. of pure 2-methoxy-4-nitrobenzoyl chloride.[2b] When the addition was completed, the resulting suspension was stirred for 15 minutes, filtered and the insoluble product was washed thoroughly with water and dried at 70°. The finely powdered, crude material was stirred at 50° for 15 minutes with 500 ml. of 5% aqueous sodium hydroxide solution and the insoluble material was filtered, washed thoroughly with water and recrystallized twice from glacial acetic acid; *cf.* Table VI.

2-Ethoxy-4-nitrobenzamide.—A mixture of 32 g. (0.166 mole) of 2-ethoxy-4-nitrobenzonitrile[11] and 100 ml. of concentrated sulfuric acid was stirred and heated until the temperature of the mixture was 97°. The heat source was removed; the internal temperature spontaneously rose to 109°. When the internal temperature had dropped to 95°, the mixture was held at 96–97° for a further 1-hr. period. After quenching in 500 ml. of water, the insoluble product was filtered off, washed thoroughly with water and dried at 80°. Three recrystallizations from absolute alcohol furnished 13 g. (37%) of the pure 2-ethoxy-4-nitrobenzamide.

2-Butoxy-4-nitrobenzamide.—General method for alkoxy groups larger than ethoxy: The preparation of 2-butoxy-4-nitrobenzoyl chloride was carried out in benzene solution in the presence of pyridine.[2b] The resulting benzene suspension was added slowly to an excess of concentrated ammonium hydroxide solution, with vigorous stirring. The emulsion was filtered and the insoluble material was washed well with water. The benzene layer was separated from the filtrate and washed with water; evaporation gave a small additional amount of product. The combined fractions, after three recrystallizations from ethyl acetate, gave a 67% yield of pure 2-butoxy-4-nitrobenzamide.

4-Amino-2-alkoxybenzamides.—The reduction of the 2-alkoxy-4-nitrobenzamides was carried out either by means of iron–hydrochloric acid in dilute alcohol[2a] or by catalytic reduction with platinum oxide in alcoholic solution. The yields were good in all cases (80–95%).

RENSSELAER, NEW YORK

[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

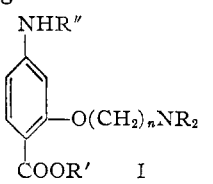
Derivatives of 4-Amino-2-hydroxybenzoic Acid. V. Basic Ethers

BY R. O. CLINTON, S. C. LASKOWSKI, U. J. SALVADOR AND PATRICIA M. CARROLL

RECEIVED OCTOBER 15, 1956

A series of alkyl 4-amino-2-(dialkylaminoalkoxy)-benzoates was prepared for testing as potential local anesthetics. The compounds proved to be good local anesthetics; of more interest was the observation that quaternary salts of these compounds exhibited a high degree of activity as ganglionic blocking agents.

Previous communications[1] from these laboratories have described basic esters, thiol esters and amides derived from 4-amino-2-hydroxybenzoic acids. In these compounds, either the carboxyl or the 4-amino group served as a linkage point for the attachment of a dialkylaminoalkyl chain, which was introduced to confer local anesthetic activity. A third point of attachment for the basic moiety, *viz.*, the 2-hydroxy group, is considered in the present communication. These compounds have the general structure shown by I.



I

Although a compound of type I has not appeared in the literature, a number of related des-amino and des-carboxy analogs have been reported. Chapman, *et al.*,[2] prepared bis-diethylaminoethoxy compounds derived from stilbestrol and hexylresorcinol. Peak and co-workers[3] synthesized several series of basic ethers derived from various chlorinated phenols, catechol, hydroquinone, etc. Furthermore Einhorn and Rothlauf[4] have prepared several alkyl 2- and 4-(2-diethylaminoethoxy)-benzoates and phenolic monobasic ethers, and Rohmann and Friedrich[5] reported the preparation of 4-(2-diethylaminoethoxy)-aniline and a number of its derivatives. In most of these cases pharmacological data have not been reported for the compounds.

Reference should also be made to the dialkylaminoalkoxyaryl compounds and related benzodioxane derivatives, which have been extensively studied by Bovet and co-workers[6] and found to have a wide variety of pharmacodynamic activities.

The alkyl 4-amino-2-(dialkylaminoalkoxy)-benzoates prepared during this investigation were tested for local anesthetic activity[7] by standard methods. In general the compounds were highly active in the intracutaneous wheal and sciatic nerve block tests but less active as corneal local anesthetics. Increasing the side chain length (*e.g.*, from 2-(2-diethylaminoethoxy)- to 2-(3-diethylaminopropoxy)-) or altering the terminal basic moiety (*e.g.*, from dimethylamino to 2-methyl-1-piperidyl) produced a substantial increase in activity. Similarly, changing the ester group from methyl to butyl increased the subcutaneous local anesthetic activity moderately and the topical (corneal) activity markedly. The

(1) (a) R. O. Clinton, S. C. Laskowski, U. J. Salvador, Mary Wilson, Helen Bates and Patricia Carroll, THIS JOURNAL, **73**, 3674 (1951); (b) **74**, 592 (1952); (c) **76**, 5121 (1954); (d) **79**, 2285 (1957).

(2) C. W. Chapman, G. P. Hager and D. E. Shay, *J. Am. Pharm. Assoc.*, **36**, 78 (1947).

(3) D. J. Drain, D. A. Peak and F. F. Whitmore, *J. Chem. Soc.*, 2680 (1949); J. L. Lowe, D. A. Peak and T. I. Watkins, *ibid.*, 3286 (1951).

(4) A. Einhorn and L. Rothlauf, *Ann.*, **382**, 237 (1911); *cf.* C. Rohmann and B. Scheurle, *Arch. Pharm.*, **274**, 110 (1936).

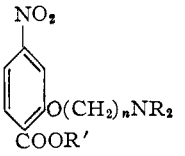
(5) C. Rohmann and K. Friedrich, *Ber.*, **72**, 1333 (1939).

(6) D. Bovet and A. Simon, *Compt. rend. soc. biol.*, **117**, 958 (1934); subsequent papers by D. Bovet, E. Zinz, J. Levy and I. A. M. Staub.

(7) F. P. Luduena and J. O. Hoppe, to be published.

TABLE I

ALKYL 2-(DIALKYLAMINOALKOXY)-4-NITROBENZOATES



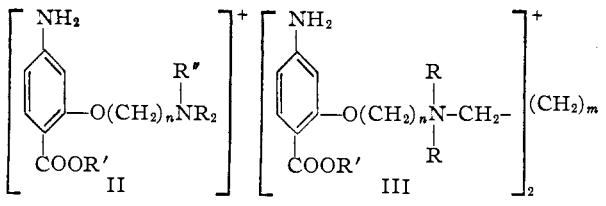
n	R_2	R'	M.p., °C.	Hydrochloride Formula	Hydrochloride Nitrogen, % Calcd.	Hydrochloride Nitrogen, % Found	Hydrochloride Chlorine, % Calcd.	Hydrochloride Chlorine, % Found	Picrate M.p., °C.	Picrate Nitrogen, % Calcd[a]	Picrate Nitrogen, % Found[a]
2	$(CH_3)_2$	C_2H_5	202.2–202.6	$C_{13}H_{19}ClN_2O_5$	8.79	8.56	11.12	11.10	139.4–140.4	10.96	10.88
2	$(C_2H_5)_2$	CH_3	156.9–159.2	$C_{14}H_{21}ClN_2O_5$	8.42	8.38	10.65	10.50	149.8–150.6	10.68	10.79
2	$(C_2H_5)_2$	C_2H_5	143.9–144.8	$C_{15}H_{23}ClN_2O_5$	4.04[a]	3.79[a]	10.22	10.21	137.8–139.0	10.40	10.18
2	$(C_2H_5)_2$	n-C_3H_7	153.4–155.4	$C_{16}H_{25}ClN_2O_5$	7.77	7.95	9.83	9.83	98.8–100.6	10.12	10.01
2	$(C_2H_5)_2$	n-C_4H_9	117.6–118.6	$C_{17}H_{27}ClN_2O_5$	7.47	7.66	9.46	9.44	120.5–121.6	9.88	9.78
3	$(C_2H_5)_2$	C_2H_5	164.8–165.6	$C_{16}H_{25}ClN_2O_5$	7.77	7.87	9.83	9.72	98.6–99.2	10.12	10.07
2	$(i$-$C_3H_7)_2$[b]	C_2H_5	169.1–170.7	$C_{17}H_{27}ClN_2O_5$	7.47	7.26	9.46	9.40	160.3–163.2	9.87	9.89
2	C_4H_8O[c]	CH_3	206.0–206.4	$C_{14}H_{19}ClN_2O_6$	4.04[a]	4.05[a]	10.22	10.21	161.6–162.2	10.40	10.22
2	C_4H_8O[c]	C_2H_5	207.0–208.0	$C_{15}H_{21}ClN_2O_6$	7.77	7.81	9.83	9.92	154.8–155.6	10.12	10.02
3	C_4H_8O[c]	C_2H_5	142.0–144.6	$C_{16}H_{23}ClN_2O_6$	7.47	7.79	9.46	9.25	133.4–134.2	9.88	9.74
2	C_5H_{10}[d]	C_2H_5	191.0–191.5	$C_{16}H_{23}ClN_2O_5$	7.81	7.82	9.88	9.90	141.7–142.9	10.16	10.02
3	C_5H_{10}[d]	C_2H_5	160.4–161.6	$C_{17}H_{25}ClN_2O_5$	7.52	7.37	9.51	9.33	139.6–140.4	9.92	10.18
2	C_6H_{12}[e]	C_2H_5	180.8–182.6	$C_{17}H_{25}ClN_2O_5$	7.52	7.22	9.51	9.38	138.0–139.0	9.92	9.97
3	C_6H_{12}[e]	C_2H_5	158.2–159.6	$C_{18}H_{27}ClN_2O_5$	7.24	7.03	9.16	8.92	104.6–108.8	9.68	9.65
2	C_7H_{14}[f]	C_2H_5	153.0–154.0	$C_{18}H_{27}ClN_2O_5$	7.24	7.15	9.16	9.14	207.6–209.0	9.68	9.58

[a] N[a], see ref. 10. [b] The base melted at 42.0–48.9°. Calcd.: N, 8.28. Found: N, 8.35. [c] 4-Morpholinyl. [d] 1-Piperidyl. [e] 2-Methyl-1-piperidyl. [f] 2,6-Dimethyl-1-piperidyl.

compounds were, in general, somewhat more toxic and slightly more irritating than their basic ester counterparts[1a,b] and therefore had lower therapeutic indices. Several of the 4-amino compounds possessed a fair degree of oral analgesic activity (*cf.* reference 1d).

The alkyl 4-alkylamino-2-(dialkylaminoalkoxy)-benzoates (I, R″ = butyl, 5-hydroxyamyl, etc.), like their basic ester counterparts,[1a,b] were *less* active than their 4-amino precursors, both subcutaneously and topically (contrast: procaine *vs.* tetracaine). Moreover, the 4-alkylamino derivatives were considerably more irritating than their 4-amino precursors; for this reason only a few examples of the series were prepared. Removal of the ester group with the formation of I (R = H) destroyed all activity.

During the course of the present investigation several quaternary salts derived from I were also prepared (*cf.* II). These quaternary salts, as well as their corresponding 4-nitro precursors, were found to be highly active as ganglionic blocking agents.[8] The series was therefore extended to



II

III

include a large number of representatives of II, as well as bisquaternary salts of type III (m = 0–4). Most of these compounds were very active, the greatest activity being found with compounds wherein R′ was propyl or butyl, and R and R″ were small (methyl, ethyl, etc.). Activity decreased markedly with the series shown in III as the value of m increased.

The alkyl 2-(dialkylaminoalkoxy)-4-nitrobenzoates were prepared in several ways. The direct reaction between an alkyl 2-hydroxy-4-nitrobenzoate and a dialkylaminoethyl chloride (a modified Horenstein–Pählicke reaction) gave the desired products, although in poor yields. The yields were considerably lower than those obtained previously from 2-hydroxy-4-nitrobenzonitrile[9] by the use of this reaction, indicating the pronounced steric effect of the carbalkoxy grouping.[1a] Moreover, the reaction failed completely with 3-dialkylaminopropyl chlorides, even in the presence of added iodide ion. Considerably better yields were obtained by condensation of sodio-phenolate with a dialkylaminoalkyl chloride in an anhydrous alcoholic solution or in toluene; use of the latter solvent was mandatory with highly reactive halides such as 2-dimethylaminoethyl chloride and in general was the most useful reaction medium.

The route from ethyl 2-(2-chloroethoxy)-4-nitrobenzoate *via* condensation with a secondary amine was also investigated; here again poor overall yields were obtained. The alkyl 2-(dialkylaminoalkoxy)-4-nitrobenzoates as well as their characterizing derivatives, are summarized in Table I.

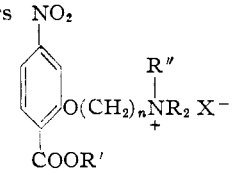
The alkyl 2-(dialkylaminoalkoxy)-4-nitrobenzoate quaternary salts, listed in Table II, were prepared by the direct condensation of the free base with an alkyl halide or an α,ω-dibromoalkane. Steric effects were quite pronounced. The size of the ester group had no apparent effect since there appeared to be no difference in the rates of reaction of the methyl, ethyl, propyl or butyl esters with, *e.g.*, methyl iodide. The size of the entering R″

(8) J. O. Hoppe, to be published.

(9) R. O. Clinton and S. C. Laskowski, THIS JOURNAL, **74**, 2226 (1952).

TABLE II

ALKYL 2-(DIALKYLAMINOALKOXY)-4-NITROBENZOATE QUATERNARY SALTS



n	R_2	R'	R''	X	M.p., °C.	Formula	Analyses, % N Calcd.[a]	N Found[a]	X Calcd.[b]	X Found[b]
2	$(CH_3)_2$	C_2H_5	CH_3	I	190.2–191.2	$C_{14}H_{21}IN_2O_5$	6.60[c]	6.38[c]	29.92	30.10
2	$(CH_3)_2$	C_2H_5	C_2H_5	I	119.1–120.2	$C_{15}H_{23}IN_2O_5$	3.19	3.22	28.96	28.82
2	$(CH_3)_2$	C_2H_5	i-C_3H_7	Br	180.1–182.4	$C_{16}H_{25}BrN_2O_5$	3.46	3.49	19.71	19.75
2	$(CH_3)_2$	C_2H_5	i-C_4H_9	Br	137.4–148.2	$C_{17}H_{27}BrN_2O_5$	3.34	3.36	19.06	18.62
2	$(CH_3)_2$	C_2H_5	i-C_5H_{11}	Br	150.6–153.0	$C_{18}H_{29}BrN_2O_5$	3.22	3.24	18.44	18.70
2	$(CH_3)_2$	C_2H_5	$-CH_2CH_2OH$	Br	129.7–138.0	$C_{15}H_{23}BrN_2O_6$	3.44	3.59	[d]	[d]
2	$(CH_3)_2$	C_2H_5	C_7H_7[e]	Br	153.3–155.1	$C_{20}H_{25}BrN_2O_5$	3.09	2.98	17.63	17.80
2	$(CH_3)_2$	C_2H_5	C_8H_{15}[f]	Br	121.9–123.5	$C_{21}H_{33}BrN_2O_5$	[g]	[g]	16.88	16.72
2	$(CH_3)_2$	C_2H_5	$-(CH_2)_2-$[h]	Br	164.1–172.0	$C_{28}H_{40}Br_2N_4O_{10}$	3.72	3.76	21.24	21.24
2	$(CH_3)_2$	C_2H_5	$-(CH_2)_3-$[h]	Br	185.1–192.0	$C_{29}H_{42}Br_2N_4O_{10}$	3.65	3.61	20.85	20.42
2	$(CH_3)_2$	C_2H_5	$-(CH_2)_4-$[h]	Br	179.0–186.9	$C_{30}H_{44}Br_2N_4O_{10}$	3.59	3.52	20.48	20.10
2	$(CH_3)_2$	C_2H_5	$-(CH_2)_5-$[h]	Br		$C_{31}H_{46}Br_2N_4O_{10}$	3.52	3.46	20.12	19.78
2	$(CH_3)_2$	C_2H_5	$-(CH_2)_6-$[h]	Br	192.3–195.9	$C_{32}H_{48}Br_2N_4O_{10}$	3.47	3.35	19.77	19.61
2	$(C_2H_5)_2$	CH_3	CH_3	I	162.5–163.0	$C_{15}H_{23}IN_2O_5$	3.19	3.22	28.96	28.80
2	$(C_2H_5)_2$	C_2H_5	CH_3	Br	150.6–151.6	$C_{16}H_{25}BrN_2O_5$	3.45	3.41	19.72	19.66
2	$(C_2H_5)_2$	C_2H_5	CH_3	I	143.1–144.6	$C_{16}H_{25}IN_2O_5$	6.20[c]	6.16[c]	28.06	28.15
2	$(C_2H_5)_2$	n-C_3H_7	CH_3	I	143.2–144.6	$C_{17}H_{27}IN_2O_5$	3.00	3.04	27.22	27.00
2	$(C_2H_5)_2$	n-C_4H_9	CH_3	I	118.2–120.3	$C_{18}H_{29}IN_2O_5$	2.92	3.11	26.42	26.30
2	$(C_2H_5)_2$	C_2H_5	C_2H_5	I	140.7–141.9	$C_{17}H_{27}IN_2O_5$	3.00	3.02	27.22	27.01
2	$(C_2H_5)_2$	C_2H_5	$-(CH_2)_2-$[h]	Br	146.7–148.7	$C_{32}H_{48}Br_2N_4O_{10}$	3.47	3.50	19.77	20.18
2	$(C_2H_5)_2$	C_2H_5	$-(CH_2)_4$[h]	Br	143.2–146.8	$C_{34}H_{52}Br_2N_4O_{10}$	3.35	3.57	19.11	19.37
2	$(C_2H_5)_2$	C_2H_5	$-(CH_2)_6$[h]	Br	150.7–158.2	$C_{36}H_{56}Br_2N_4O_{10}$	3.24	3.14	18.49	18.21
3	$(C_2H_5)_2$	C_2H_5	CH_3	I	148.0–149.6	$C_{17}H_{27}IN_2O_5$	3.00	3.10	27.22	27.30
2	$(i$-$C_3H_7)_2$	C_2H_5	CH_3	I	183.7–184.2	$C_{18}H_{29}IN_2O_5$	2.91	2.90	26.42	26.18
2	C_4H_8O[i]	CH_3	CH_3	I	209.0–211.0	$C_{15}H_{21}IN_2O_6$	3.09	3.17	28.06	27.88
2	C_4H_8O[i]	C_2H_5	CH_3	I	190.5–191.3	$C_{16}H_{23}IN_2O_6$	3.00	3.02	27.22	26.90
3	C_4H_8O[i]	C_2H_5	CH_3	I	161.1–161.7	$C_{17}H_{25}IN_2O_6$	2.92	2.91	26.42	26.33
2	C_5H_{10}[k]	C_2H_5	CH_3	I	147.7–148.9	$C_{17}H_{25}IN_2O_5$	3.02	3.03	27.34	26.92
3	C_5H_{10}[k]	C_2H_5	CH_3	I	166.9–167.9	$C_{18}H_{27}IN_2O_5$	2.93	2.99	26.53	26.30
2	C_6H_{12}[l]	C_2H_5	CH_3	I	159.8–161.0	$C_{18}H_{27}IN_2O_5$	2.93	2.92	26.53	26.22
3	C_6H_{12}[l]	C_2H_5	CH_3	I	165.5–166.5	$C_{19}H_{29}IN_2O_5$	2.85	2.87	25.78	25.44
2	C_7H_{14}[m]	C_2H_5	CH_3	I	192.3–192.9	$C_{19}H_{29}IN_2O_5$	2.85	2.82	25.78	25.40

[a] See ref. 10. [b] Bromide ion on bromides; iodide ion on iodides. [c] Total nitrogen. [d] Calcd.: C, 44.23; H, 5.69. Found: C, 43.95; H, 5.64. [e] Benzyl. [f] β-Cyclohexylethyl. [g] Calcd.: C, 53.28; H, 7.02. Found: C, 53.03; H, 7.30. [h] Bis-quaternary. [i] M.p. dependent upon immersion point; when immersed at 25° sintered from 152°, melted at 184–187° dec. [j] 4-Morpholinyl. [k] 1-Piperidyl. [l] 2-Methyl-1-piperidyl. [m] 2,6-Dimethyl-1-piperidyl.

group and of the R_2 group(s) (*cf.* II), however, had a marked effect. When NR_2 was 2-methyl-1-piperidyl, for example, the rate of reaction with methyl iodide was only about one-tenth as fast as the reaction with the analogous nitro base wherein NR_2 was diethylamino. Reactions of the α,ω-dibromoalkanes with compounds which contained 2-dimethylaminoethoxy groups took place at a moderate rate in boiling acetonitrile; reaction with compounds which contain 2-diethylaminoethoxy groups was very slow even in boiling nitromethane.

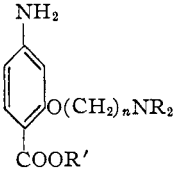
In addition to the picrates of the alkyl 2-(dialkylaminoalkoxy)-4-nitrobenzoates listed in Table I, several 2-cyano-5-nitrophenolates were also synthesized for comparison with the analogous 2-(dialkylaminoalkoxy)-4-nitrobenzonitrile 2-cyano-5-nitrophenolates.[9] Although an extensive series of these salts was not prepared in the present work, it is of interest that the molecular compounds formed are apparently greatly influenced by steric effects, as was previously noted.[9] Ethyl 2-(2-diethylaminoethoxy)-4-nitrobenzoate, similar to 2-(2-diethylaminoethoxy)-4-nitrobenzonitrile, yielded a di-(2-cyano-5-nitrophenolate). On the other hand, both ethyl 2-(3-(1-piperidyl)-propoxy)- and ethyl 2-(3-(4-morpholinyl)-propoxy)-4-nitrobenzoates gave di-(2-cyano-5-nitrophenolates), whereas the analogous benzonitriles gave *mono* salts. The spectra of the ethyl 2-(dialkylaminoalkoxy)-4-nitrobenzoate 2-cyano-5-nitrophenolates were similar to those found for the corresponding benzonitriles.[9]

The alkyl 4-amino-2-(dialkylaminoalkoxy)-benzoates were prepared by iron–hydrochloric acid reduction of the nitro compounds. The bases were obtained crystalline in most cases; they were characterized as their phosphoric and picric acid salts. These compounds are summarized in Table III.

The alkyl 4-amino-2-(dialkylaminoalkoxy)-

TABLE III

ALKYL 4-AMINO-2-(DIALKYLAMINOALKOXY)-BENZOATES

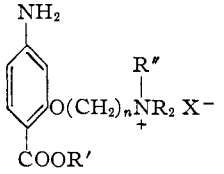


					Phosphate				Picrate		
					Nitrogen, %		H_3PO_4, %			Nitrogen, %	
n	R_2	R'	M.p., °C.	Formula	Calcd.	Found	Calcd.	Found	M.p., °C.	Calcd.[a]	Found[a]
2	$(CH_3)_2$	C_2H_5[b]	176.3–177.3	$C_{13}H_{23}N_2O_7P$	8.00	7.98	27.98	28.10	140.2–141.2	5.82	5.53
2	$(C_2H_5)_2$	CH_3	195.8–196.8	$C_{14}H_{25}N_2O_7P$	7.69	7.61	26.91	27.10	119.0–120.4[c]	11.60[d]	11.39[d]
2	$(C_2H_5)_2$	C_2H_5[e]	168.7–169.6	$C_{15}H_{27}N_2O_7P$	7.40	7.41	25.91	25.30	131.6–133.2	8.43[d]	8.25[d]
2	$(C_2H_5)_2$	n-C_3H_7	153.0–154.0	$C_{16}H_{29}N_2O_7P$	7.14	7.15	24.99	25.23	140.4–141.2	5.36	5.23
2	$(C_2H_5)_2$	n-C_4H_9	154.5–155.5	$C_{17}H_{31}N_2O_7P$	6.88	7.10	24.12	24.15	120.8–122.6	5.22	5.08
3	$(C_2H_5)_2$	C_2H_5	151.5–153.2	$C_{16}H_{29}N_2O_7P$	7.14	7.05	24.99	25.00	146.2–147.0	5.36	5.27
2	$(i$-$C_3H_7)_2$	C_2H_5	186.0–187.0	$C_{17}H_{31}N_2O_7P$	3.44[a]	3.42[a]	24.12	24.70	196.8–197.8[f]	5.15[g]	5.36[g]
2	C_4H_8O[h]	CH_3[i]	151.3–152.1	$C_{14}H_{26}N_2O_{12}P_2$	5.88	5.96	41.16	40.85	168.5–169.7	13.75[j]	13.56[j]
2	C_4H_8O[h]	C_2H_5[k]	196.3–196.9	$C_{15}H_{25}N_2O_8P$	7.14	7.16	24.99	24.50	165.8–166.8	5.35	5.09
3	C_4H_8O[h]	C_2H_5[l]	143.3–144.4	$C_{16}H_{27}N_2O_8P$	6.88	6.65	24.12	24.00	210.4–211.4	5.21	4.95
2	C_5H_{10}[m]	C_2H_5[n]	220.8–221.4	$C_{16}H_{27}N_2O_7P$	7.18	7.17	25.11	25.41	159.0–160.0	5.37	5.07
3	C_5H_{10}[m]	C_2H_5[o]	160.2–161.6	$C_{17}H_{29}N_2O_7P$	6.93	6.83	24.22	24.37	218.0–218.7	5.23	5.07
2	C_6H_{12}[p]	C_2H_5[q]	.....	.....	..	..	...	...	172.4–173.6	5.23	5.18
3	C_6H_{12}[p]	C_2H_5[r]	136.4–138.3	$C_{18}H_{31}N_2O_7P$	6.70	6.56	23.43	23.12	180.8–183.0	5.10	5.16
2	C_7H_{14}[s]	C_2H_5	211.0–211.8	$C_{18}H_{31}N_2O_7P$	6.70	6.67	23.43	23.60	188.8–189.6	5.10	4.88

[a] N_{AP} except as noted; *cf.* ref. 10. [b] The base melted at 94.2–95.6°. Calcd.: N, 11.11. Found: N, 11.14. [c] Dipicrate. [d] N^a, see ref. 10. [e] The dihydrochloride had m.p. 173.6–173.9°. Calcd. for $C_{15}H_{26}Cl_2N_2O_3$: C, 50.99; H, 7.42; Cl, 20.07. Found: C, 51.14; H, 7.36; Cl, 19.90. [f] Flavianate. [g] Sulfur analysis. [h] 4-Morpholinyl. [i] Diphosphate. [j] Total nitrogen. [k] The base had m.p. 98.0–99.8°. Calcd.: N, 9.52. Found: N, 9.42. [l] The base had m.p. 106.8–108.0°. Calcd.: N, 9.09. Found: N, 8.78. [m] 1-Piperidyl. [n] The base had m.p. 107.3–108.5°. Calcd.: N, 9.58. Found: N, 9.40. [o] The base had m.p. 109.2–110.1°. Calcd.: N, 9.14. Found: N, 8.90. [p] 2-Methyl-1-piperidyl. [q] The base had m.p. 91.2–92.4°. Calcd.: N, 9.14. Found: N, 9.26. [r] The base had m.p. 112.4–113.8°. Calcd.: N, 8.74. Found: N, 8.54. [s] 2,6-Dimethyl-1-piperidyl.

TABLE IV

ALKYL 4-AMINO-2-(DIALKYLAMINOALKOXY)-BENZOATE QUATERNARY SALTS



							Nitrogen, %		X, %	
n	R_2	R'	R''	X	M.p., °C.	Formula	Calcd.	Found	Calcd.[a]	Found[a]
2	$(CH_3)_2$	C_2H_5	CH_3	I	204.2–205.2	$C_{14}H_{23}IN_2O_3$	7.10	7.13	32.19	31.78
2	$(CH_3)_2$	C_2H_5	C_2H_5	I	172.3–175.3	$C_{15}H_{25}IN_2O_3$	6.86	6.78	31.09	31.03
2	$(CH_3)_2$	C_2H_5	i-C_3H_7	Br	190.0–192.2	$C_{16}H_{27}BrN_2O_3$	7.46	7.39	21.29	21.28
2	$(CH_3)_2$	C_2H_5	CH_2CH_2OH	Br	138.9–142.3	$C_{15}H_{25}BrN_2O_4$	7.42	7.42	21.18	21.20
2	$(CH_3)_2$	C_2H_5	C_8H_{15}[b]	Br	101.6–105.1	$C_{21}H_{35}BrN_2O_3$	6.31	6.23	18.02	17.85
2	$(CH_3)_2$	C_2H_5	$-(CH_2)_2-$[c]	Br	190.0–195[d]	$C_{28}H_{44}Br_2N_4O_6$	8.09	8.01	23.08	23.20
2	$(CH_3)_2$	C_2H_5	$-(CH_2)_4-$[c]	Br	150[e]	$C_{30}H_{48}Br_2N_4O_6$	7.77	7.64	22.18	21.78
2	$(CH_3)_2$	C_2H_5	$-(CH_2)_5-$[c]	Br	125[f]	$C_{31}H_{50}Br_2N_4O_6$	7.62	7.38	21.76	21.50
2	$(CH_3)_2$	C_2H_5	$-(CH_2)_6-$[c]	Br	200.7–202.5	$C_{32}H_{52}Br_2N_4O_6$	7.48	7.26	21.35	20.90
2	$(C_2H_5)_2$	CH_3	CH_3	I	127.4–129.0	$C_{15}H_{25}IN_2O_3$	6.86	7.00	31.09	31.50
2	$(C_2H_5)_2$	C_2H_5	CH_3	Br	160.3–162.1	$C_{16}H_{27}BrN_2O_3$	7.46	7.49	21.29	20.95
2	$(C_2H_5)_2$	C_2H_5	CH_3	I	139.2–141.1	$C_{16}H_{27}IN_2O_3$	[g]	[g]	30.05	29.70
2	$(C_2H_5)_2$	n-C_3H_7	CH_3	I	127.4–129.6	$C_{17}H_{29}IN_2O_3$	6.42	6.52	29.09	28.91
2	$(C_2H_5)_2$	n-C_4H_9	CH_3	I	88.2–92.4	$C_{18}H_{31}IN_2O_3$	6.22	6.33	28.18	28.00
2	$(C_2H_5)_2$	C_2H_5	C_2H_5	I	141.2–143.8	$C_{17}H_{29}IN_2O_3$	6.42	6.30	29.09	28.94
3	$(C_2H_5)_2$	C_2H_5	CH_3	I	125.0–126.0	$C_{17}H_{29}IN_2O_3$	6.42	6.35	29.09	29.03
2	C_4H_8O[h]	C_2H_5	CH_3	I	182.7–183.7	$C_{16}H_{25}IN_2O_4$	6.42	6.40	29.09	29.12
3	C_4H_8O[h]	C_2H_5	CH_3	I	151.9–153.1	$C_{17}H_{27}IN_2O_4$	6.22	6.25	28.18	28.13
2	C_5H_{10}[i]	C_2H_5	CH_3	I	167.4–168.4	$C_{17}H_{27}IN_2O_3$	6.45	6.30	29.22	29.41
3	C_5H_{10}[i]	C_2H_5	CH_3	I	150.1–150.6	$C_{18}H_{29}IN_2O_3$	6.25	6.09	28.31	28.61
2	C_7H_{14}[j]	C_2H_5	CH_3	I	123.4–126.4	$C_{19}H_{31}IN_2O_3$	6.06	5.84	27.45	27.59

[a] Bromide ion on bromides; iodide ion on iodides. [b] β-Cyclohexylethyl. [c] Bis-quaternary. [d] With decomposition. [e] M.p. indefinite above 160° with decomposition. [f] M.p. indefinite, above 190° dec. [g] Calcd.: C, 45.50; H, 6.45. Found: C, 45.28; H, 6.58. [h] 4-Morpholinyl. [i] 1-Piperidyl. [j] 2,6-Dimethyl-1-piperidyl.

benzoate quaternary salts were prepared by the catalytic reduction of the nitro-quaternary salts in the appropriate alcohol as solvent. In a number of cases the 4-amino-quaternary salts could not be obtained crystalline; those which were characterized are listed in Table IV.

Experimental[10]

Alkyl 2-(Dialkylaminoalkoxy)-4-nitrobenzoates.—Several synthetic methods, described below, were used for the preparation of the alkyl 2-(dialkylaminoalkoxy)-4-nitrobenzoates. The compounds prepared are listed in Table I.

Method A.—To a warm solution of 39.4 g. (0.20 mole) of methyl 2-hydroxy-4-nitrobenzoate in 1400 ml. of dry toluene there was added a solution prepared from 4.6 g. (0.20 mole) of sodium and 500 ml. of absolute methanol. The methanol was distilled from the stirred suspension until a constant distillation temperature of 110° was reached. To the red suspension was added 29.8 g. (0.22 mole) of 2-diethylaminoethyl chloride in 500 ml. of dry toluene, and the mixture was stirred and refluxed for 20 hr.; during this period the color faded to pale yellow. The mixture was cooled, filtered, and the insoluble material was washed thoroughly with dry benzene. Distillation of the solvents *in vacuo* left an oily residue of methyl 2-(2-diethylaminoethoxy)-4-nitrobenzoate. Conversion to the hydrochloride was effected by treatment of an ethyl acetate solution of the crude base with an excess of ethereal hydrogen chloride; after one recrystallization from absolute methanol–ethyl acetate, there was obtained an 85% yield of pure material.

This method could be used for the preparation of the majority of the esters in Table I by substituting the appropriate sodium alkoxide–alcohol mixture (depending upon the ester employed) for the sodium methoxide–methanol. The yields were high and as much as two moles of a 2-hydroxy ester could be alkylated by this method on a laboratory scale.

Method B.—A mixture of 24.7 g. (0.11 mole) of propyl 2-hydroxy-4-nitrobenzoate, 16.3 g. (0.12 mole) of 2-diethylaminoethyl chloride and 250 ml. of *n*-propyl alcohol was refluxed and stirred for 8 hr. After the usual procedure there was obtained 1.0 g. of pure propyl 2-(2-diethylaminoethoxy)-4-nitrobenzoate hydrochloride, m.p. and mixed m.p. 153–155°. The yield was not increased by prolonged refluxing.

Method C.—Ethyl 2-hydroxy-4-nitrobenzoate was alkylated by 2-chloroethyl *p*-toluenesulfonate in the usual manner.[1b] **Ethyl 2-(2-chloroethoxy)-4-nitrobenzoate** crystallized from *n*-hexane in pale yellow platelets, m.p. 56.6–57.2°.

Anal. Calcd. for $C_{11}H_{12}ClNO_5$: Cl, 12.96. Found: Cl, 12.62.

When refluxed with an ethanolic solution of a secondary amine in the presence of sodium iodide, there were obtained 50–65% yields of the corresponding ethyl 2-(2-dialkylaminoethoxy)-4-nitrobenzoates.

Method D.—The reaction between an alkyl 2-hydroxy-4-nitrobenzoate, sodium alkoxide and a dialkylaminoalkyl chloride in an alcohol under anhydrous conditions was carried out by substantially the same procedure used with 2-hydroxy-4-nitrobenzonitrile.[9] The only modification necessary was the use of the appropriate alcohol as solvent for the reaction. The effect of the alcohol was indicated by the following yield data, utilizing 2-diethylaminoethyl chloride in each case: methyl ester in methanol: (5%); ethyl ester in ethanol: (71%), propyl ester in *n*-propyl alcohol: (88%); butyl ester in *n*-butyl alcohol: (86%); methyl ester in ethanol: (70%) of *ethyl* ester basic ether (by transesterification).

Alkyl 2-(Dialkylaminoalkoxy)-4-nitrobenzoate Quaternary Salts.—The quaternary salts were prepared in every case from the pure base (liberated from the pure hydrochloride). The following methods were used.

Method A (Methiodides, Methobromides).—To a solution of the base in ethyl acetate, under anhydrous conditions, was added three moles of methyl iodide or bromide. The initially deep orange-colored solution rapidly or slowly changed in color to pale yellow as crystals deposited. After 3–20 hr. at room temperature, the mixture was filtered and the precipitate was washed thoroughly with ethyl acetate. Recrystallization from absolute alcohol or an isopropyl alcohol–ethyl acetate mixture gave a pure quaternary salt.

Ethyl iodide reacted quantitatively with ethyl 2-(2-dimethylaminoethoxy)-4-nitrobenzoate under these conditions, but no product was obtained with the 2-(2-diethylaminoethoxy) homolog at room temperature.

Method B (Alkyl Bromides).—A solution of the base in acetonitrile was mixed with three moles of the alkyl bromide and the mixture was refluxed for 36–72 hr. In the preparation of the bis-quaternaries derived from ethyl 2-(2-dimethylaminoethoxy)-4-nitrobenzoate, similar conditions were used except that a 2.4-to-1 mole ratio of base to the α,ω-dibromoalkane was used. The latter conditions also applied to the preparation of the bis-quaternaries derived from ethyl 2-(2-diethylaminoethoxy)-4-nitrobenzoate which were prepared using nitromethane as solvent; the mixtures were refluxed for 48–72 hr.

Alkyl 2-(Dialkylaminoalkoxy)-4-nitrobenzoate 2-Cyano-5-nitrophenolates.—The 2-cyano-5-nitrophenolate derivatives were prepared[9] from 0.01 mole of the alkyl 2-(dialkylaminoalkoxy)-4-nitrobenzoate and 0.02 mole of 2-hydroxy-4-nitrobenzonitrile, in ethyl acetate solution. The yields were essentially quantitative.

Ethyl 2-(2-diethylaminoethoxy)-4-nitrobenzoate di-(2-cyano-5-nitrophenolate), canary yellow prisms, m.p. 76.0–78.0°. *Anal.* Calcd. for $C_{29}H_{30}N_6O_{11}$: N^a, 6.58; N_{AP}, 2.19. Found: N^a, 6.59; N_{AP}, 2.19.

Ethyl 2-(3-(1-piperidyl)-propoxy)-4-nitrobenzoate di-(2-cyano-5-nitrophenolate), short, blunt orange needles, m.p. 125.2–126.0; λ^{alc}_{max} 234 (inflection), 265, 338, 406 mμ (ϵ 36,800, 27,770, 8,510, 2,100, respectively).

Anal. Calcd. for $C_{31}H_{32}N_6O_{11}$: N^a, 6.32; N_{AP}, 2.11. Found: N^a, 6.20; N_{AP}, 2.12.

Ethyl 2-(3-(4-morpholinyl)-propoxy)-4-nitrobenzoate di-(2-cyano-5-nitrophenolate), hair-like yellow-orange needles, m.p. 137.2–138.3°; λ^{alc}_{max} 234 (inflection), 265,340 mμ (ϵ 28,200, 25,000, 9,510, respectively). *Anal.* Calcd. for $C_{30}H_{30}N_6O_{12}$: N^a, 6.30; N_{AP}, 2.10. Found: N^a, 6.49; N_{AP}, 2.16.

2-(2-Diethylaminoethoxy)-4-nitrobenzoic Acid.—A mixture of 15.0 g. (0.043 mole) of ethyl 2-(2-diethylaminoethoxy)-4-nitrobenzoate hydrochloride, 18.3 g. (0.17 mole) of sodium carbonate and 200 ml. of 50% alcohol was stirred and refluxed for 4 hr. The alcohol was removed *in vacuo* and, after filtration, the aqueous residue was acidified to congo red paper with concentrated hydrochloric acid and saturated with ammonium sulfate. The precipitate was filtered and dried *in vacuo* at 70°; yield 13.8 g. (98%), m.p. 211–213°. Recrystallization from methanol gave the pure compound with but little loss, m.p. 212.5–213.9°.

Anal. Calcd. for $C_{13}H_{19}ClN_2O_5$: C, 48.98; H, 6.01; Cl, 11.12; N^a, 4.39. Found: C, 49.28; H, 6.13; Cl, 10.92; N^a, 4.21.

A mixture of 31.9 g. (0.1 mole) of the above hydrochloride, 8.4 g. (0.1 mole) of sodium bicarbonate and 500 ml. of absolute alcohol was stirred and refluxed for 3 hr., cooled, filtered and the filtrate was evaporated to dryness *in vacuo*. Recrystallization from isopropyl alcohol gave 25.0 g. of 2-(2-diethylaminoethoxy)-4-nitrobenzoic acid, m.p. 164.6–166.6°.

Anal. Calcd. for $C_{13}H_{18}N_2O_5$: N_{AP}, 4.97. Found: N_{AP}, 4.93.

The picrate crystallized from alcohol in cottony yellow needles, m.p. 179.2–180.4°. *Anal.* Calcd. for $C_{19}H_{21}N_5O_{12}$: N, 13.70. Found: N, 13.48.

2-(2-Dimethylaminoethoxy)-4-nitrobenzoic acid, prepared by the above method, formed cream colored plates from absolute alcohol, m.p. 193.1–194.1°. *Anal.* Calcd. for $C_{11}H_{14}N_2O_5$: N^a, 5.51. Found: N^a, 5.51.

The hydrochloride crystallized from absolute alcohol in pale yellow needles; m.p. 208.0–209.6°. *Anal.* Calcd. for $C_{11}H_{15}ClN_2O_5$: N^a, 4.82; Cl, 12.20. Found: N^a, 4.70; Cl, 12.06.

(10) All melting points are corrected; they were determined in a modified Hershberg apparatus using total immersion N.B.S. calibrated thermometers. The analyses were done by Mr. M. E. Auerbach, Mr. K. D. Fleischer, and their staffs; absorption spectra by Dr. F. C. Nachod and staff. N^a is used to indicate nitro nitrogen, by titration with titanous chloride; N_{AP} indicates basic nitrogen by titration with perchloric acid; N. E. indicates neutral equivalent, by titration with sodium methoxide.

The picrate was prepared by treating an aqueous solution of the hydrochloride with an excess of a saturated aqueous picric acid solution; clusters of yellow needles, m.p. 181.8–182.6°. *Anal.* Calcd. for $C_{17}H_{17}N_5O_{12}$: N^a, 11.60. Found: N^a, 11.51.

2-(3-(1-Piperidyl)-propoxy)-4-nitrobenzoic acid hydrochloride, pale yellow cottony needles from absolute alcohol, m.p. 216.8–217.5°. *Anal.* Calcd. for $C_{15}H_{21}ClN_2O_5$: N, 8.16; Cl, 10.28. Found: N, 8.17; Cl, 10.09.

The picrate, canary yellow needles from absolute alcohol, m.p. 143.0–145.0°. *Anal.* Calcd. for $C_{21}H_{23}N_5O_{12}$: N^a, 10.43. Found: N^a, 10.10.

Alkyl 4-Amino-2-(dialkylaminoalkoxy)-benzoates.—The alkyl 2-(dialkylaminoalkoxy)-4-nitrobenzoate bases or hydrochlorides were reduced by the iron–hydrochloride acid method,[1a] in the appropriate dilute alcohol as solvent, or by catalytic reduction of the hydrochloride (platinum oxide, 25°, alcohol solvent). The crystalline 4-amino bases were recrystallized from benzene or an ethyl acetate–*n*-hexane mixture. The bases did not readily yield crystalline mono- or dihydrochlorides, but the phosphates were easily prepared.[1a,9] The picrates were prepared in the usual manner, using an excess of picric acid. These compounds are listed in Table III.

Alkyl 4-Amino-2-(dialkylaminoalkoxy)-benzoate Quaternary Salts.—The reduction of the alkyl 2-(dialkylaminoalkoxy)-4-nitrobenzoate quaternary salts and bis-quaternary salts was carried out catalytically, using platinum oxide as catalyst, the appropriate alcohol or dilute alcohol as solvent, a temperature of 25° and a pressure of 40 lb. The products were isolated in the usual manner, utilizing a vacuum distillation with ethyl acetate for dehydration prior to crystallization from isopropyl alcohol–ethyl acetate or absolute alcohol. A number of the 4-amino quaternary salts could not be obtained crystalline; in certain cases these were tested as the crude oils. The crystalline 4-amino quaternary salts are listed in Table IV.

4-Amino-2-(dialkylaminoalkoxy)-benzoic Acids.—The 2-(dialkylaminoalkoxy)-4-nitrobenzoic acids or their hydrochlorides were reduced catalytically by the above method.

4-Amino-2-(2-dimethylaminoethoxy)-benzoic acid hydrochloride, white needles from absolute alcohol, m.p. 145.5–147.2° dec. *Anal.* Calcd. for $C_{11}H_{17}ClN_2O_3$: N, 10.75; Cl, 13.60. Found: N, 10.74; Cl, 13.93.

4-Amino-2-(2-diethylaminoethoxy)-benzoic acid, white needles, m.p. 158.0–158.8° dec. *Anal.* Calcd. for $C_{13}H_{20}N_2O_3$: C, 61.88; H, 7.99; N, 11.11. Found: C, 61.88; H, 7.76; N, 11.05.

The picrate, canary yellow needles from alcohol, m.p. 187.5–188.3°. *Anal.* Calcd. for $C_{19}H_{23}N_5O_{10}$: N_{AP}, 5.82. Found: N_{AP}, 5.52.

4-Amino-2-(3-(1-piperidyl)-propoxy)-benzoic acid hydrochloride, tan needles, m.p. 162.1–162.8° dec. *Anal.* Calcd. for $C_{15}H_{23}ClN_2O_3$: N, 8.90; Cl, 11.26. Found: N, 9.20; Cl, 10.96.

4-Alkylamino-2-(dialkylaminoalkoxy)-benzoates.—The reductive alkylation of the 4-amino bases by means of an aldehyde, zinc dust and acetic acid was carried out as previously described.[1a,b]

Ethyl 4-butylamino-2-(2-diethylaminoethoxy)-benzoate hydrochloride, cream-colored needles from absolute alcohol–ethyl acetate, m.p. 160.5–161.8°. *Anal.* Calcd. for $C_{19}H_{33}ClN_2O_3$: N, 7.51; Cl, 9.50. Found: N, 7.36; Cl, 9.45.

The flavianate, yellow-orange plates from alcohol, m.p. 164.6–165.6°. *Anal.* Calcd. for $C_{29}H_{38}N_4O_{11}S$: S, 4.92. Found: S, 4.96.

Ethyl 4-(5-hydroxyamylamino)-2-(2-diethylaminoethoxy)-benzoate hydrochloride, white cottony needles from absolute alcohol–*n*-hexane, m.p. 132.2–133.4°. *Anal.* Calcd. for $C_{20}H_{35}ClN_2O_4$: N, 6.95; Cl, 8.79. Found: N, 7.07; Cl, 9.05.

The flavianate, cottony orange needles, m.p. 126.0–126.4°. *Anal.* Calcd. for $C_{30}H_{40}N_4O_{12}S$: S, 4.71. Found: S, 4.47.

Ethyl 4-(2,2-dimethyl-3-hydroxypropylamino)-2-(2-(2,6-dimethyl-1-piperidyl)-ethoxy)-benzoate, white needles from benzene, m.p. 90.0–91.0°. *Anal.* Calcd. for $C_{23}H_{38}N_2O_4$: C, 67.94; H, 9.42; N, 6.89. Found: C, 68.06; H, 9.31; N, 6.81.

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[CONTRIBUTION NO. 228 FROM JACKSON LABORATORY, E. I. DU PONT DE NEMOURS AND CO., INC.]

Preparation of N,N'-Disubstituted *p*-Quinonediimine-N,N'-dioxides

BY C. J. PEDERSEN

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Several members of a new class of compounds (I, where R and R' are alkyl or aryl groups which may or may not be identical) have been prepared by treating either VI or VII with an excess of perbenzoic acid. They are highly colored compounds whose solutions in organic solvents are very sensitive to light. Many of them are good inhibitors of free radical polymerization as well as efficient inhibitors of autoxidation.

During a study of the action of perbenzoic acid on N,N'-disubstituted derivatives of *p*-phenylenediamine, products were obtained which were found to belong to a new class of compounds having structure I.[1] The closest references in the literature are to N-phenyl-*p*-quinoneimine-N-oxide (II),[2] 5,6-bis-(phenylimino)-2-cyclohexene-1,4-dione-N,N'-dioxide (III)[3] and phenazine-N,N'-dioxide (IV).[4]

The two methods of preparing these compounds are shown in Fig. 2. Method I consists in treating one mole of N,N'-disubstituted *p*-quinonediimine (VI) with slightly more than two moles of perbenzoic acid, and method II of treating one mole of N,N'-disubstituted *p*-phenylenediamine (VII) with a little more than three moles of perbenzoic acid.

N-Substituted *p*-nitroanilines (VIII) are obtained as by-products in method II when R or R', or both, are unsubstituted alkyl groups. The group which comes off the nitrogen atom is always the unsubstituted alkyl group. When both R and R' are substituted *t*-alkyl or aromatic groups, no derivative of *p*-nitroaniline is formed to any extent.

The establishment of the structure of these compounds is based mainly on work with N,N'-diphenyl-*p*-quinonediimine-N,N'-dioxide. The molecular weight and the elementary analyses of this compound are consistent with the composition of I (R and R' = phenyl), and its structure is indicated by its hydrogenation to N,N'-diphenyl-*p*-phenylenediamine (VII R and R' = phenyl).

It is an orange, crystalline compound whose solutions are very sensitive to light.[5] Its visible spectrum, shown in Fig. 3 has a peak at 417 mμ, ε 47,000. Structure X (R and R' = phenyl) is

(1) C. J. Pedersen, United States Patent 2,681,918, June 22, 1954; *C. A.*, **49**, 7595 (1955).

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(3) W. Gündel and R. Pummer, *Ann.*, **529**, 11 (1937).

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