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Identification of Organic Compounds. II. Piperidyl Derivatives of Aromatic Halogenonitro Compounds[1]

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The work of this Laboratory on the systematic identification of organic compounds has been extended to the development of standard procedures for the preparation of derivatives of aromatic halogenonitro compounds by means of their reaction with piperidine. This paper reports the results of a study of thirty-seven members of this class. In addition to the application of standard procedures, it includes other observations which are of assistance in identifying the compounds as well as the optimum conditions for preparation and the characterization of all their possible piperidyl derivatives.

As a reagent for the preparation of derivatives of compounds with reactive halogen atoms, piperidine possesses many advantages over other bases such as ammonia, aromatic amines, alkali alkoxides[4] or morpholine.[5] Its main advantage lies in its far greater reactivity, a fact shown quantitatively by workers such as Franzen and Bockhacker[6] and Harradence and Lions.[5] Moreover the main reaction products tend to be more readily crystallized and in general contain fewer by-products.

In preparing piperidyl derivatives no single method applicable to all halogenonitro compounds can be used, both because of the spread in the reactivities of halogen atoms in variously substituted compounds and because of the fact that in certain cases two or more halogen atoms can be replaced successively by careful control of conditions. However, two fairly general reactions have been developed: *i. e.*, procedure A in which the compound is refluxed with piperidine for one hour and procedure B in which an alcohol solution is heated fifteen minutes on the steam-bath. Procedure A yielded derivatives in 65% and identifiable compounds in 79% of the thirty-seven cases studied, the difference in the percentages representing recoveries of original material. The corresponding figures for procedure B are 46 and 74%, respectively.

Initial evidence for the reactivity of the compounds was gained by observing the phenomena occurring on adding piperidine to the solid. Such observations are often valuable in suggesting the identity of an unknown halogenonitro compound. The mildest conditions of time, temperature and solvent for the complete replacement of each halogen atom were determined so that a qualitative comparison of the reactivities of these halogen atoms might be made.

In certain cases replacement of a nitro group in preference to a halogen atom occurs, as Mangini and Deliddo and Le Fèvre and Turner have already shown for the ortho dinitro compounds 19[7,8] and 13.[4] Such replacement is often evidenced by the initial red or red-orange color of the solution of the compound in piperidine and by the failure of any piperidine hydrohalide to precipitate even though the solution boils. The nitro group splits out as nitrosopiperidine for the residual clear yellow oil gives the diphenylamine test for nitrosamines. The presence of this compound in the reaction mixture seems to exert a catalytic effect in continued piperidination because dipiperidination of 13 and 19 occurs more readily than dipiperidination of 15 and 22, which yield the same derivatives, respectively. Although 27 also possesses two nitro groups ortho to each other, successive replacement of the chlorine atoms is the chief result of the reaction.[9] Compound 26 whose structure is intermediate between those of 13 and 27 resembles each of them to a certain extent so that derivatives formed by replacement of one nitro group or of two chlorine atoms were isolated.[10] The somewhat similar

(1) For Articles I and III, see THIS JOURNAL, **62**, 511, 603 (1940).

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(4) Le Fèvre and Turner, *J. Chem. Soc.*, 1113–1122 (1927).

(5) Harradence and Lions, *J. Proc. Roy. Soc. N. S. Wales*, **70**, 406–412 (1937).

(6) Franzen and Bockhacker, *Ber.*, **53**, 1174–1179 (1920).

(7) These numbers refer to those assigned the compounds in Tables I and II.

(8) Mangini and Deliddo, *Gazz. chim. ital.*, **63**, 625 (1933).

(9) Some nitro replacement is evidenced by the following facts: nitroso piperidine was detected even in the mildest reactions, crude samples of the dipiperidyl derivative always possessed low broad melting points and the piperidine hydrochloride yield was never higher than 80% for two chlorine atoms replaced.

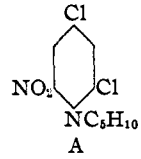
(10) Replacement of chlorine (in preference to nitro) by piperidyl in 26 and 27 is contrary to the results reported for the reaction of these compounds with ammonia; see MacLeod, Pfund and Kilpatrick, THIS JOURNAL, **44**, 2268 (1922), Körner, *Gazz. chim. ital.*, **4**, 353 (1874), and Blanksma, *Rec. trav. chim.*, **27**, 47 (1908).

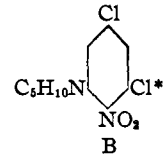
trinitro compound, 21, however, shows only replacement of the 2-nitro group. Which of the two ortho nitro groups is replaced does not seem to follow any rule as far as can be determined from the compounds under observation. In fact, their reactivities are often so nearly alike that the main reaction product is definitely contaminated with a product resulting from replacement of the other nitro group.[11] Para nitro groups also may be replaced as evidenced by 25.

Preparation of all the theoretically possible piperidyl derivatives of each compound was successful in every case with the exception of the monopiperidyl derivative of 32 and the tripiperidyl derivatives of 30 and 33. The derivatives are for the most part readily crystallizable solids melting between 30 and 225°. Some have already been reported as shown in Table I; others, shown in Table II, are new.

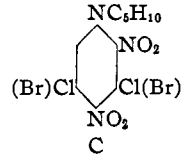
The structures of fifteen of the twenty-two new compounds as well as of one already reported may be considered established either by proof, by formation due to replacement of all the halogen in the original compound or replacement of all the halogen atoms which are ortho or para to a nitro group[12] or by evidence as to whether a chlorine atom or a nitro group has been replaced. The structures of the remaining seven compounds as well as of one already reported (the monopiperidyl derivative of 16) are open to some doubt. Footnotes in Table II indicate the assumed structures, whose tentative assignment is based on such facts as the proved structures of amino derivatives of the same halogenonitrobenzenes, the greater reactivity toward amines of halogen ortho to nitro in contrast to halogen para to nitro, and the tendency of the known symmetrical derivatives to be higher melting and more insoluble.

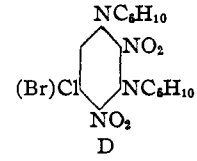
The structures newly established in this work include the following. The identity of the mono- and dipiperidyl derivatives of 19 and 22 limits their structures to N-(3-chloro-6-nitrophenyl)-piperidine and 1-nitro-2,4-di-N-piperidylbenzene. Similarly, 21 and 24 produce the same derivative, indicating that the 2-nitro in 21 is reactive. The monopiperidyl derivative of 26, which forms by replacement of a nitro group, might be either A or B


A

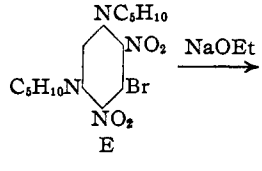

B

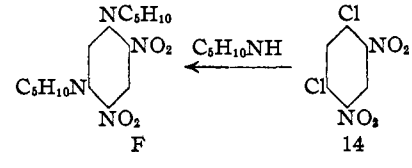
It appears to be A as the molecule contains no further reactive chlorine; the Cl* in formula B should be reactive. Also B is believed to be the structure of the monopiperidyl derivative of 30, a compound which melts 15° lower and contains another reactive chlorine atom. The question of the order of replacement of the halogen atoms in the symmetrical trihalogenodinitrobenzenes 16 and 17 has finally been definitely established, at least in respect to the replacement of bromine in 17 by piperidyl. The monopiperidyl derivatives of 16 and 17 already reported have been assigned structure C.[4,13]


C


D

The dipiperidyl derivatives have never been prepared before although analogous compounds have been obtained with other amines.[13,14] Borsche's work[13] seemed to show indirectly that the di derivatives were of type D. However, E is definitely the structure of the bromodipiperidyl compound since by reduction with sodium ethylate, similar to the work of Jackson on the establishment of the structures of the two diethoxy derivatives of 17,[15] F is produced which is the known dipiperidyl derivative of 14.


E


F 14

(11) For example, the crude mono- and dipiperidyl derivatives of 19 melt low and over a wide range and the maximum yield of piperidine hydrochloride obtained in the preparation of the latter was 80% no matter how extended the time of reaction. That the presence of nitrosopiperidine in the reaction mixture is not the cause of this reduced yield is proved by the fact that the symmetrical compound 13 produces 100% piperidine hydrochloride yields. Such facts indicate that some replacement of the 4-nitro group accompanies the main replacement of the 3-nitro group.

(12) The complete non-reactivity of halogen atoms meta to nitro groups toward all reagents has been well established.

(13) Borsche and Trautner, *Ann.*, **447**, 1–18 (1926).

(14) Hüffer, *Rec. trav. chim.*, **40**, 451–476 (1921).

(15) Jackson and Warren, *Am. Chem. J.*, **13** 164–193 (1891); Jackson and Koch, *ibid.*, **21**, 510–528 (1899).

This work also proves that C is the structure of the monopiperidyl of 17. The structures of the derivatives of the chloro analog 16 may be assumed to be C and E, respectively, an assumption supported by the similarity in properties, although a reduction such as described above could not be carried out.

The meta substituted compound 20 is characteristically different from all the compounds studied, for it dissolves in piperidine without change in temperature but with the formation of a black-red color. The deep color is believed to be caused by the formation of a molecular addition product since addition of water to a newly mixed solution reprecipitates the original.[16] However, no crystalline addition compound could be isolated. The reaction of *sym*-trinitrobenzene was investigated and found to give analogous results although in this case an unstable mole for mole addition complex could be crystallized.[17] In both cases further deep-seated reactions occur between the nitrobenzene and excess piperidine if allowed to stand or if heated; from the resultant brown powders with indefinite melting points no pure products could be isolated readily.

Experimental

All melting points reported in this paper were taken by the method described in Mulliken's "Identification of Pure Organic Compounds," Vol. I, page 218, on a 360° melting point thermometer immersed in sulfuric acid to the 0° point. All melting points are uncorrected.

Procedure A.—To 0.5 g. of the halogenonitro compound add 1.5 ml. (1.0 ml. for bromo compounds) of piperidine.[18] Observe phenomena such as sputtering (stir to prevent local overheating), boiling, color formation and the time elapsing before piperidine hydrohalide precipitates; these are partially dependent on the quantities used. Reflux the resultant solution or mixture in an oil-bath for one hour, cool, add water and filter. If the product separates as an oil, the following crystallization methods should be tried in order[19]: (a) ice the mixture for an hour with scratching (with few exceptions this method is sufficient); (b) decant the aqueous layer containing excess piperidine and piperidine hydrohalide and wash the oil several times with water; (c) freeze in dry-ice. If no crystallization is then obtained, abandon the experiment. The yields are 90–100% and the crude product will melt sharply provided that the chlorine replacement is complete and decomposition products due to excessive reactivity are not present.

Recrystallize from 85% alcohol using excess if the melting point is low. Certain high melting insoluble compounds require 95% alcohol, acetone, or glacial acetic acid; such cases are mentioned in the footnotes of Table II.

The by-product piperidine hydrohalide yield, an index of the completeness of the reaction, can be determined qualitatively by evaporating the aqueous filtrate of the crude product and weighing the residue. If a nitro group is replaced, this residue is a reddish, acetone-soluble gum, giving a nitrosamine test with diphenylamine reagent.

Procedure B.—Dissolve 0.5 g. of the compound in 5 ml. of boiling alcohol (more if necessary), add 1.5 ml. (1.0 ml. for bromo compounds) of piperidine and heat for fifteen minutes on the steam-bath. If the product does not separate on cooling or icing, force it out with water, crystallizing any oil obtained as described above. If water has not been added before filtering, wash the precipitate with water to remove possible contaminating piperidine hydrohalide. The yields are only 70–90%, but the crystallization from alcohol effects purification.

Modified Procedures.—In most cases the standard procedures do not represent the readiest method of obtaining the derivatives of any one compound, nor can all the theoretically possible derivatives of each compound be prepared by these means. Therefore, modified procedures have been developed. For the most part these consist of applying conditions A or B with a change in the time of heating. These times are noted in Tables I and II; for example, A-2h means that conditions A should be applied for two hours (m is used to represent minutes) and B-0m means that as soon as the piperidine is added to the hot alcohol solution of the compound, the mixture is allowed to cool. The exact number of minutes is critical only in cases where the first of two reactive

(16) Although no addition compounds of 20 and amines have been reported, *m*-dinitrobenzene and certain of its derivatives are known to yield them: see Pfeiffer, "Organische Molekülverbindungen," 1927, p. 360.

(17) Romburgh, *Rec. trav. chim.*, **14**, 68 (1895), obtained the color but could not crystallize the compound.

(18) Monsanto catalytic piperidine with a reboiling range of 104–107° was used for this investigation; see Cook, THIS JOURNAL, **59**, 2661 (1937).

(19) The more laborious crystallization aids suggested by Le Fèvre and Turner,[4] are unnecessary. In fact the ability to dissolve readily in dilute hydrochloric acid is confined to those piperidyl derivatives with few ring substituents.

TABLE I

NEW DATA ON KNOWN PIPERIDYL DERIVATIVES[a]

No.	Halogenated nitrobenzenes[b]	Type of deriv.	Usable[c] stand. proc.	Readiest prepn.[d]
1, 2	1-Chloro- and 1-bromo-2-	Mono[e]	A	A-20m(Cl) A-10m(Br)
3, 4	1-Chloro- and 1-bromo-3-	None	Orig. recov.	
5, 6	1-Chloro- and 1-bromo-4-	Mono[f,g]	A	A-2h(Cl) A-30m(Br)
7, 8	1-Chloro- and 1-bromo-2,4-di-	Mono[f,h,i]	A, B	B-0m[j]
9	1-Chloro-2,6-di-[k]	Mono[l]	A, B	B-0m[j]
10	1-Chloro-2,4,6-tri	Mono[f,m]	B	B-0m[j]
11	1,2-Dichloro-4-	Mono[g]	A	A-20m
12	1,4-Dichloro-2-	Mono[e(1),i]	A	A-20m
13	1,2-Dichloro-4,5-di-[g]	Mono[g]		E-1m[j]
14	1,3-Dichloro-4,6-di-[n]	Mono[g,o]		2M-B-0m[j]
		Di[g]	A, B	B-0m
15	1,2,4-Trichloro-5-[p,q]	Mono[g]		D
16	1,3,5-Trichloro-2,4-di[q,r]	Mono[s]		2M-B-5m
		Tri[g,s,t]	A	A-20m
17	1,3,5-Tribromo-2,4-di-[q,u]	Mono[g,v]		B-2m
		Tri[g,s,t]	A	A-10m
18	*p*-Nitrobenzyl chloride	Mono[w]	A, B	C-2m

[a] In most cases the melting points of the derivatives obtained checked those reported within 2°; wider discrepancies are noted. Compounds 19, 22, 28, 36, and 37, which yielded results completely at variance with the literature, are listed in Table II. Compounds 13, 15, 16, and 17 are in both Tables I and II. [b] Eastman Kodak Co. material unless otherwise stated. [c] "Usable" means that the crude product will be crystalline and purifiable by a maximum of two recrystallizations. [d] Easiest and quickest way of obtaining a pure derivative. Represents the mildest conditions for complete halogen replacement except when footnoted *j*. See Experimental Section for explanation of symbols. [e] (1) Lellmann and Geller, *Ber.*, **21**, 2281–2287 (1888). (2) M. p. 77–77.5°, recorded, [81°]. [f] "Beilstein," Vol. XX, p. 22. [g] Ref. 4. [h] Ref. 20. [i] Fox and Turner, *J. Chem. Soc.*, 1853–1867 (1930). [j] Complete replacement of the halogen occurs at once, *i. e.*, under conditions E-1m. [k] Sane and Joshi, *J. Indian Chem. Soc.*, **9**, 60 (1932). [l] Borsche and Rantscheff, *Ann.*, **379**, 166 (1911). [m] 95% alcohol is preferable for recrystallization. [n] Obtained from Fraenkel and Landau. [o] Borsche and Bahr, *Ann.*, **402**, 96 (1914). M. p. 114–114.5°, recorded, [117–118°, 119°]. *Anal.* Calcd. for $C_{11}H_{12}ClN_3O_4$: Cl, 12.4. Found: Cl, 12.4, 12.5. [p] Beilstein and Kurbatow, *Ann.*, **192**, 230 (1878); Holleman and Van Haeften, *Rec. trav. chim.*, 40, 70 (1921). [q] Carten, Ph.D. Thesis, Massachusetts Institute of Technology, 1939, pp. 116–118. [r] Ref. 14. [s] Ref. 13. [t] Glacial acetic acid is preferable for recrystallization. M. p. 183–184°, recorded, [177–178°, 147–148°]. *Anal.* Calcd. for $C_{21}H_{31}N_5O_4$: N, 16.8. Found: N, 16.9, 16.9. [u] Jackson, *Ber.*, **8**, 1172 (1875). [v] M. p. 129–129.5°, recorded, [125–126°]. [w] Lellmann and Pekrun, *Ann.*, **259**, 40 (1890). Best purified by dissolving in 95% alcohol and adding water dropwise so that the oil crystallizes as it forms.

chlorine atoms is being replaced; otherwise it represents the minimum time required for complete halogen replacement as evidenced by piperidine hydrohalide yields. Other procedures are as follows: C, mix the two reactants and add water after the specified time, this representing the simplest method of obtaining a derivative; D, add ice-cold piperidine to the solid compound also iced, continue icing until the initial violent reaction has moderated and then allow the mixture to stand in a water-bath maintained at room temperature, stirring frequently, until the spontaneous evolution of heat ceases (one to two hours); E, dissolve the compound in the least amount of cold alcohol (20–40 ml. for 0.5 g.), add piperidine and after the specified time at room temperature add water to precipitate the product. To prepare monopiperidyl derivatives in cases where dipiperidination is rapid, the amount of piperidine must be limited to the exactly calculated two mols; such procedures are prefixed by 2M. Calculated quantities may be used in other cases to conserve piperidine.

Structure Proofs. Monopiperidyl Derivatives of 1-Chloro-2,3,5-trinitrobenzene (21) and 1,2-Dichloro-3,5-dinitrobenzene (24).—By replacement of a nitro group in 21 a piperidyl derivative was obtained which did not lower the melting point of the monopiperidyl derivative of 24 (which was formed by replacement of a chlorine). Therefore the derivatives must be N-(2-chloro-4,6-dinitrophenyl)-piperidine.

Derivatives of 1-Chloro-3,4-dinitrobenzene (19) and 1,3-Dichloro-4-nitrobenzene (22).—The mono- and dipiperidyl derivatives of 19, formed, respectively, by replacement of one nitro group and a nitro group plus a chlorine, do not lower the melting points of the corresponding derivatives of 22 formed by successive replacements of the chlorines. Therefore, the 3-nitro must be

TABLE II

PREPARATION AND PROPERTIES OF PIPERIDYL DERIVATIVES

No.	Halogenated nitrobenzene[a]	Derivative Pos. of NC_5H_{10}	Formula	Analysis, % Calcd.	Found[b]	Usable[a] stand. proc.	Readiest prepn.[a]	M. p., °C. (uncor.)	Color	Crystal form
19	1-Chloro-3,4-di-[c]	3	$C_{11}H_{12}ClN_3O_2$	Cl, 14.7	14.9	B[d]	E-30m	69–70[e]	Orange	Diamonds
		1, 3	$C_{16}H_{22}N_3O_2$	N, 14.5	14.4		A-4h	77.5–78.5[e]	Yel.-or.	Needles
20	1-Chloro-3,5-di-[f]	See discussion								
21	1-Chloro-2,3,5-tri-[g]	2	Same as 24			A, B	B-0m,[h] C-1m			
22	1,3-Dichloro-4-[i]	3	Same as 19[e]			A, B	C-30m			
		1, 3	Same as 19[e]				A-12h			
23	1,3-Dichloro-5-[j,k]	None formed[l]				Orig. recov.				
24	1,2-Dichloro-3,5-di-[k,m]	2	$C_{11}H_{12}ClN_3O_4$	Cl, 12.4	12.5	A, B	B-0m[h] C-1m	125.5	Yellow	Sheets
13	1,2-Dichloro-4,5-di-[n]	2, 4	Same as 15, see below			A	A			
25	1,3-Dichloro-2,5-di-[g]	2[o]	$C_{11}H_{12}Cl_2N_2O_2$	Cl, 25.8	25.9	A, B	B-0m	86.5–87.5	Yellow	Needles
26	1,3-Dichloro-4,5-di-[k,p]	4	$C_{11}H_{12}Cl_2N_2O_2$	Cl, 25.8	25.8		[q]	57–58	Golden	Plates
		1, 3	$C_{16}H_{22}N_4O_4$	N, 16.7	16.7		[r]	173–173.5	Orange	Ferns
27	1,4-Dichloro-2,3-di-[s]	1	$C_{11}H_{12}ClN_3O_4$	Cl, 12.4	12.4		B-2m	91–92	Red.-or.	Needles
		1, 4	$C_{16}H_{22}N_4O_4$	N, 16.7	16.8	A	A-5m	167–167.5[t]	Crimson	Plates
28	1,4-Dichloro-2,6-di-[s]	1	$C_{11}H_{12}ClN_3O_4$	Cl, 12.4	12.4	A, B	C-1m B-0m[h]	71.5–72.5[u]	Scarlet	Needles
29	1,2,3-Trichloro-4-[v,w]	3[x]	$C_{11}H_{12}Cl_2N_2O_2$	Cl, 25.8	26.1		A-2m	73–74	Orange	Needles
		1, 3	$C_{16}H_{22}ClN_3O_2$	Cl, 11.0	11.3		A-12h	93.5–94	Lemon	Diamonds
15	1,2,4-Trichloro-5-[n]	2, 4	$C_{16}H_{22}ClN_3O_2$	Cl, 11.0	11.0	A	A-2h	103.5–104[y]	Orange	Plates
30	1,3,5-Trichloro-2-[v,w]	1[z]	$C_{11}H_{12}Cl_2N_2O_2$	Cl, 25.8	25.8		[aa]	41–42	Or.-yel.	Powder
		1, 3[z]	$C_{16}H_{22}ClN_3O_4$	Cl, 11.0	11.1		A-4h	88.5–89.5	Yellow	Needles
31	1,2,3,-Trichloro-4,6-di-[w,bb]	1	$C_{11}H_{11}Cl_2N_3O_4$	Cl, 22.2	22.2		2M-B-5m	95–96	Orange	Needles
		1, 3	$C_{16}H_{21}ClN_4O_4$	Cl, 9.61	9.72	A, B	B-0m	188.5–189[t,cc]	Yellow	Cubes
32	1,2,4-Trichloro-3,5-di-[w,bb]	2, 4[dd]	$C_{16}H_{21}ClN_4O_4$	Cl, 9.61	9.48	A, B	B	142.5–143	Orange	Needles
		Stable form			9.48		[ee]	146.5–147.5	Yellow	Needles
16	1,3,5-Trichloro-2,4-di-[n]	1, 5[ff]	$C_{16}H_{21}ClN_4O_4$	N, 15.2	15.2	B	B-10m	190[t]	Lemon	Needles
33	1,3,5-Tribromo-2-[w,gg]	1[hh]	$C_{11}H_{12}Br_2N_2O_2$	Br, 43.9	44.0		A-2½m	70–71	Lemon	Powder
		1, 3[hh]	$C_{16}H_{22}BrN_3O_2$	Br, 21.7	21.7		A-2 to 3h	87.5–88	Golden	Needles
17	1,3,5-Tribromo-2,4-di-[n]	1, 5	$C_{16}H_{21}BrN_4O_4$	Br, 19.3	19.3		D	224–225[t]	Yellow	Needles
34	2-Chloro-6-nitrotoluene	None formed				Orig. recov.				
35	4-Chloro-2-nitrotoluene	None formed				Orig. recov.				
36	*o*-Nitrobenzyl chloride[ii]	ω	$C_{12}H_{16}N_2O_2$	N, 12.7	12.7	B[d]	B-0m	38–39[jj,kk]	Del. yel.	Needles
			$C_{12}H_{16}N_2O_2 \cdot HCl$	Cl, 13.8	14.0			210.5–212[kk,ll]	Colorless	Rhomb.
37	*m*-Nitrobenzyl chloride[mm]	ω	$C_{12}H_{16}N_2O_2$	Never dried		A, B[d]	C-1m	10–13[kk,nn]	Yellow	Oil
			$C_{12}H_{16}N_2O_2 \cdot HCl$	Cl, 13.8	13.8		B-0m	202.5–205[kk,ll]	Colorless	Cubes

[a] As in Table I. [b] Value reported is mean of two determinations; average deviation of analyses from means is 0.4%. [c] Fraenkel and Landau product recrystallized from 85% alcohol until air evaporation of the alcohol solution deposited crystals and not an oil. *Anal.* Calcd. for $C_6H_3ClN_2O_4$: Cl, 17.5. Found: Cl, 17.5, 17.4. [d] Dry-ice required for crystallization. [e] See discussion in Experimental Section. [f] Bader, *Ber.*, **24**, 1655 (1891), and de Kock, *Rec. trav. chim.*, **20**, 112 (1901). The 3,5-dinitroaniline necessary for the preparation was obtained preferably from 3,5-dinitrobenzoyl chloride, Blanksma and Verberg, *ibid.*, **53**, 988 (1934). [g] In the diazotization of 2,6-dichloro-4-nitraniline and the replacement of the diazo group by a nitro group according to Körner and Contardi, *Chem. Abs.*, **8**, 1761–1762 (1914), and Holleman,[k] the 5% yield of the desired 1,3-dichloro-2,5-dinitrobenzene (25) was accompanied by a 6% yield of 21, the latter being less volatile in superheated steam. It was identified by its melting point, its analysis (Calcd. for $C_6H_2ClN_3O_6$: Cl, 14.3. Found: Cl, 14.5, 14.5) and its piperidyl derivative. [h] Complete replacement of the halogen or nitro group occurs at once, *i. e.*, under conditions E-1m. [i] Roberts and Turner, *J. Chem. Soc.*, 2011 (1925). [j] Holleman, *Rec. trav. chim.*, **23**, 366 (1904). [k] Holleman and Den Hollander, *Rec. trav. chim.*, **39**, 435–480 (1920). [l] A very slow replacement of chlorine occurs, for a trace of piperidine hydrochloride was present in the reaction mixture of procedure A, but its yield amounted to only 10% even after heating four hours. [m] Ullmann and Sané, *Ber.*, **44**, 3734 (1911). [n] See Table I for other derivatives, etc. [o] Structure assumed by analogy with mono-amino derivative, Körner and Contardi, *Chem. Abs.*, **8**, 1762 (1914). [p] Blanksma, *Rec. trav. chim.*, **27**, 46 (1908). [q] Isolated in maximum yield of 15% by recrystallizing once or twice from a large volume of 85% alcohol the oil or gummy solid obtained from conditions E-24h. [r] Isolated in maximum yield of 10% by treating the oil obtained under conditions C-10m with boiling 85 or 95% alcohol until the last few bits of oil crystallized in the hot solution and by allowing the solution to cool slowly. In one case the monopiperidyl derivative separated in a 10% yield from the filtrate after the dipiperidyl derivative had been removed. [s] Page and Heasman, *J. Chem. Soc.*, 3247–3255 (1923). [t] Glacial acetic acid is preferable for recrystallization. [u] Compare with the melting point given by Groves, Turner and Sharp, *J. Chem. Soc.*, 521 (1929). [v] Beilstein and Kurbatow, *Ann.*, **192**, 228–240 (1878). [w] Carten, Ph.D. Thesis, Massachusetts Institute of Technology, 1939, pp. 116–118. [x] Structure assumed by analogy with the mono-amino derivative.[w] [y] The crude product precipitates with piperidine of crystallization and melts around 125°; this is removed by heating for one hour at 110° or by repeated recrystallizations. [z] Structure assumed; compare with derivatives of 33. [aa] Isolated in a 70% yield by recrystallization of the oily product obtained under conditions 2M-A-20m; dry-ice cooling necessary to initiate crystallization even when pure. [bb] Reference **14**. [cc] Acetone is preferable for recrystallization. [dd] No monopiperidyl derivative could be obtained; reactions even under the mildest conditions and with only two moles of piperidine produced gums from which only the dipiperidyl derivative

could be isolated in a crystalline state. [ee] By heating the 143° compound for one hour at 125–130° or by remelting it. The 147° compound reverts to the 143° compound on recrystallization. [ff] Structure assumed by analogy with 17. See discussion. [gg] Jackson, *Ber.*, **8**, 1172–1173 (1875). [hh] Structure assumed by analogy with diamino derivative, Körner, *Gazz. chim. ital.*, 4, 425 (1874). [ii] Fraenkel and Landau material. [jj] If the product is recrystallized from 65% alcohol, a seed must be preserved to initiate crystallization; if it is recrystallized from 60% acetone and seeded by the crust which forms on the edge during icing, it must be filtered ice-cold as in the presence of acetone at room temperature the crystals return to oil. [kk] Compare Lellmann and Pekrun, *Ann.*, **259**, 40–61 (1890). [ll] Recrystallized from absolute alcohol. [mm] Norris and Taylor, THIS JOURNAL, **46**, 756 (1924). [nn] Taken floating in water.

replaced first in 19 and the 3-chloro in 22, followed by the 1-chloro in both. The properties of these derivatives (melting point and color) disagree with those already reported. Mangini[8] only obtained the monopiperidyl derivative of 19 as an oil whose hydrochloride melted at 147–150° (a crude sample of the latter prepared in this work melted at 145–149°). The dipiperidyl derivative of 22 has been described twice by Le Fèvre and co-workers[4,20] as red-orange, m. p. 67–68°; these properties as well as the method of preparation are more consistent with those given in Table II for the monopiperidyl derivative.

Monopiperidyl Derivative of 1,3-Dichloro-4,5-dinitrobenzene (26).—Analysis showed that piperidyl had replaced nitro. When 20 mg. of this derivative was subjected to the treatment A-4h, it was quantitatively recovered in pure form, m. p. 56–57° [57–58°], and did not lower the melting point of the analyzed sample; the filtrate contained only the merest traces of ionized chlorine. Therefore, this derivative contains no replaceable chlorine and must possess Structure A. Under the same conditions the monopiperidyl derivative of 30, m. p. 41–42°, and believed to possess structure B, yielded the dipiperidyl derivative which melted at 89–89.5° after one recrystallization [88.5–89.5°] and did not lower the melting point of an analyzed sample.

Mono- and Dipiperidyl Derivatives of 1,3,5-Tribromo-2,4-dinitrobenzene (17).—The structures of these derivatives were proved to be C and E, respectively, by the following reduction of the dipiperidyl derivative with sodium ethylate to F. The dipiperidyl derivative (0.5 g., 0.0012 mole) was dissolved by heating in 50 ml. of absolute alcohol and treated with 0.27 g. of sodium (10 × 0.0012 mole) dissolved in 10 ml. of absolute alcohol. The yellow solution was refluxed on the steam-bath for fifteen minutes, the color changing very slowly at first and then rapidly to orange, red and finally dark red. The dark red solution was evaporated almost to dryness by air, leached with water (which dissolved the red by-product) and filtered. The mustard colored crude (yield 50%, m. p. 120–126°) was recrystallized once or twice from 85% alcohol using Norite decolorizing carbon, m. p. 130–130.5°. Shorter reaction times, even ten minutes, produced very little reduction and, coupled with other observations, this seems to indicate that the red by-product catalyzes the reduction. Longer reaction times did not change the yields or the melting point. The identity of this product as 1,3-dinitro-4,6-di-N-piperidylbenzene was proved by a mixed melting point with authentic material, m. p. 130–131° (obtained by the action of piperidine on 14) and by analysis.

Anal. Calcd. for $C_{16}H_{22}N_4O_4$: N, 16.7. Found: N, 16.7, 16.9.

(20) Le Fèvre, Saunders and Turner, *J. Chem. Soc.*, 1171 (1927).

Dipiperidyl Derivative of 1,3,5-Trichloro-2,4-dinitrobenzene (16).—An attempt to reduce this compound to F with sodium ethylate and hence prove its structure failed. When it was subjected to the same treatment as its bromo analog (see under 17), the color change shifted only to orange-yellow after refluxing for one-half hour and a sample of the product melted at 150–165°. The ethylate concentration was tripled and the refluxing continued until the dark red color formed (three-quarter hour more). The 70% yield of product, m. p. 167–170°, crystallized from 80% acetic acid in orange-yellow needles, m. p. 173–174°. It contained no chlorine and is believed to be 1-ethoxy-2,6-dinitro-3,5-di-N-piperidylbenzene.

Anal. Calcd. for $C_{18}H_{20}N_4O_5$: N, 14.8. Found: N, 14.8, 14.9.

Lack of material prevented further investigation. The formation of this ethoxy derivative may indicate that the compound has structure D instead of E as its bromo analog, but undoubtedly the chlorine atom is more resistant to reduction than the bromine atom.

Addition Compounds with Piperidine. 1,3,5-Trinitrobenzene.—When *sym*-trinitrobenzene, m. p. 119–121, and piperidine are mixed mole for mole, a thick black-red solution forms at first with slight if any change in temperature. This thickens at once and becomes crystalline, the dark dull red product melting at 60–62° with gas evolution between 110–120°. The formation of this addition compound occurs so readily that if a few crystals of trinitrobenzene are floated on a 0.05% aqueous piperidine solution, the solution slowly acquires a very slight pink tinge. However, it is unstable in two directions. First, it decomposes into the original components whenever exposed to air, the surface fading to a light pink; solvents, while dissolving enough to produce a red solution, decompose it for the most part. Therefore it cannot be recrystallized and can be preserved only by stoppering tightly with a minimum of space. In an atmosphere saturated with piperidine it deliquesces. Second, deep-seated reactions occur slowly so that a well-stoppered sample cannot be kept for more than an hour or two before the melting point begins to drop and broaden; in three or four days the material becomes a black liquid. In fact even if the addition product were decomposed immediately

after forming, the recovered trinitrobenzene was light raspberry colored, although even two days of standing had little effect on the melting point of the recovered material. The identification of any further products was not undertaken as the material obtained from long standing or from heating the trinitrobenzene in excess piperidine consisted of brown crystallized gums, completely soluble in concentrated hydrochloric acid but not responding to any simple method of purification.

1-Chloro-3,5-dinitrobenzene (20).—This exhibited the same color phenomena with piperidine as *sym*-trinitrobenzene, but no crystalline addition product could be prepared although various ratios of piperidine to chloronitrobenzene were tried and the thick red liquids cooled in dry-ice until they hardened to glasses. This addition product does not form as readily, for although 20 deliquesces in saturated piperidine vapor, it will not produce color with aqueous piperidine. The same deep-seated reactions occur, but no pure product could be isolated from the brown powders by fractional precipitation from either the concentrated hydrochloric acid solution or from acetone solution.

Relative Reactivities.—A qualitative determination of the relative reactivities of the various compounds was made both very roughly by observing the phenomena occurring when piperidine is added to the solids and more accurately by determining the mildest conditions for complete replacement of each halogen atom as well as by certain comparative experiments not discussed. The following list is in order of decreasing reactivity in respect to monopiperidination only: A. Compounds producing sputtering as simultaneous precipitation of the piperidine hydrohalide and boiling of the red or orange liquid occurs (sp) or boiling of the red or orange solution without salt precipitation (b), (1) reactions instantaneous in cold alcohol solution [10 (sp), 7 (sp), 8 (sp), 14 (sp), 28 (sp), 24 (sp), 9 (sp), 21 (b) and 13 (b)], (2) reactions not instantaneous in cold alcohol solution, 19 (b), 25 (b), 27 (sp), [16 (sp) and 31 (sp)], 26 (b, sp), 32 (sp); B. Compounds forming clear yellow solutions from which piperidine hydrohalide precipitates in the cold in a few minutes (Xm) generally accompanied by liberation of heat, [36(0m), 37(0m) and 18(0m)], 15(0m), 17(0-1m), 22(1m), 29(1-2m), 30($2^1/_2$m), 12(5m), 33(15m); C. Compounds dissolving in piperidine with absorption of heat and producing clear yellow solutions, 2, 11, 1, 6, 5, 23, [3, 4, 34 and 35].

Summary

1. Two standard procedures for the preparation of piperidyl derivatives of aromatic halogenonitro compounds have been developed.

2. All possible piperidyl derivatives of the compounds studied have been isolated and the most favorable conditions for their preparation determined.

3. The structures of certain derivatives have been proved.

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The Deepening of Color of Sodium Nitrophenolate Solutions with Elevation of Temperature

BY TENNEY L. DAVIS AND JOSEPH L. RICHMOND

The yellow color of solutions of the salts of *m*-nitrophenol is of significance in discussions of theories of color and constitution. Satisfactory quinoid formulas may be written for the colored salts of *o*- and *p*-nitrophenol, as Armstrong[1] pointed out, and the parent substances may be supposed to exist in tautomeric quinoid forms. Hantzsch[2] accepted the view of Armstrong and suggested formulas for the colored salts of *m*-nitrophenol. Later he[3] succeeded in preparing colored and colorless esters of *o*- and *p*-nitrophenol, but not of the *m*-compound, and concluded that the free *m*-quinone is not capable of existence; or, as we should say, that *m*-nitrophenol is not capable of tautomerizing to a quinoid form, but that the colored salts of *m*-nitrophenol are nevertheless quinoid, the *m*-

(1) Armstrong, *J. Chem. Soc.*, 101 (1892).
(2) Hantzsch, *Ber.*, **39**, 1095 (1906).
(3) Hantzsch, *ibid.*, **40**, 339 (1907).