acetate thiosemicarbazone was obtained as a white solid, m.p. 151–152°; λ_{max} 221 mμ, log ϵ 4.09; λ_{max} 264 mμ, log ϵ 4.44 (methanol). The yield was 9.0 g. (56%).

Anal. Calcd. for $C_5H_{11}N_3OS$: C, 37.25; H, 6.88; N, 26.06. Found: C, 37.24; H, 6.75; N, 25.93.

When 8 g. (0.05 mole) of ethyl acetate thiosemicarbazone was heated at 180° for one hour, ethyl alcohol was evolved. The residue was extracted with 50 ml. of 1 *N* sodium hydroxide solution, and the insoluble material was collected by suction filtration. The solid was recrystallized from water and about 3 g. of 2-amino-5-methyl-1,3,4-thiadiazole (VI) was obtained as prisms, m.p. 233° dec. (lit.[5] m.p. 235°).

Anal. Calcd. for $C_3H_5N_3S$: C, 31.29; H, 4.38; N, 36.49. Found: C, 31.37; H, 4.41; N, 36.39.

The basic solution was acidified, and the resulting solid was collected. It was recrystallized from water, and about 3 g. of 3-methyl-1,2,4-triazole-5-thiol (VII) was obtained as feathery needles, m.p. 263–264° (lit.[6] m.p. 260–261°)

Anal. Calcd. for $C_3H_5N_3S$: C, 31.29; H, 4.38; N, 36.49. Found: C, 31.52; H, 4.46; N, 36.34.

2-Amino-5-ethyl-1,3,4-thiadiazole.—A mixture of 9.1 g. (0.1 mole) of thiosemicarbazide and 20 ml. of triethyl orthopropionate was heated overnight on the steam-bath. After the mixture was cooled the solid was collected and air-dried. The product was recrystallized from acetonitrile, and 2-amino-5-ethyl-1,3,4-thiadiazole was obtained as prisms, m.p. 200° (lit.[7] m.p. 198°); yield 4 g. (31%).

Anal. Calcd. for $C_4H_7N_3S$: C, 37.19; H, 5.46. Found: C, 37.35; H, 5.50.

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The S_N Mechanism in Aromatic Compounds. XVIII

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The unusual order of *ortho* substituent effects in aromatic S_N reactions previously obtained in a mononitro series,[2b] *viz.* activating power $CO_2^- < H < COPh < CO_2Me < COMe < CONH_2$, is confirmed in a similar dinitro series, except for the relative position of the parent H compound, which is associated with a constant steric hindrance due to an *ortho* NO_2 group. The activating power, both as a *para* and *ortho* substituent, of the $CONMe_2$ group has been investigated; it is normal in the former, and showing marked steric hindrance in the latter. A solvent comparison of methanol and 1/1 (v./v.) methanol–dioxane was made incidentally. The anomalous behavior of CHO and CN groups is further investigated.

Three previous papers of this series—parts VI,[2a] X[2b] and XII[3]—have dealt specifically with compounds containing CO·X (and CN) groups as *para* and *ortho* substituents in series containing also one nitro group,[2a,b] and as *para* substituents in a series containing also two nitro groups.[3]

The present paper, with reference also to a separate paper[4] dealing with some infrared investigations, is intended to complete a phase of work on such substituents by (i) confirming and amplifying the *ortho* effects shown in the mononitro series,[2a,b] (ii) confirming[2a] the source of the anomalous effects of the CN (and by analogy the CHO) group, and (iii) investigating the $CONMe_2$ group as *para* and *ortho* substituent. A comparison of the solvent effect of methanol and 1:1 (v./v.) methanol–dioxane also is made.

Data for 19 compounds are used in the Discussion, and Tables I and II list rate constants at 50°, and some derived quantities, for the replacement in these compounds of an activated Cl by OMe^- in absolute MeOH (except where stated). Some of our earlier results[2a,b,3] are included in the tables, but only the newly determined rate constants are given in the Experimental section.

TABLE I

6-SUBSTITUENT OF 1-CHLORO-2,4-DINITROBENZENE OR 4-SUBSTITUENT OF 1-CHLORO-2,6-DINITROBENZENE

Substituent	Rate constant at 0°, 10^5k_2, l. mole^{-1} sec.$^{-1}$	Substituent rate factor (S.R.F.)[5]	Steric index (S.I.)[6]	Activation (*E*), cal.	Frequency factor, $\log_{10} B$
6-H	655[a]	.....	...	170_{50}	11.5
6-H	200	1	1	174_{50}	11.2_5
4-H	4.96	1		175_{50}	9.7_5
6-CO_2^-	1.40	0.00702	1640	22000	12.9
4-CO_2^-	57.0	11.5		15500	9.2
6-$CONH_2$	5580	27.9	8·60	17200	12.5
4-$CONH_2$	1190	240		15300	10.3
6-$CONMe_2$	123[a]			20500	13.5
	[37.5][b]	[0.188]	344	[20900]	[13.2_5]
4-$CONMe_2$	322	64.7		158_{50}	10.2
6-CO_2Me	1110	5.57	131	17300	10.9
4-CO_2Me	3610	728		165_{50}	11.8
6-COPh	123	0.613	1340	17300	10.9
4-COPh	4070	821		14000	9.7

[a] For reaction with OMe^- in 1:1(v./v.) methanol–dioxane.
[b] Values in brackets estimated for reaction with OMe^- in MeOH using comparison made for 1-chloro 2,4-dinitrobenzene.

Discussion

As *para* substituents in both mono- and dinitro series the activating power of CO·X groups is in the theoretical order[2,3] $H < CO_2^- < CONH_2$ (and $CONMe_2$) $< CO_2Me < COMe < COPh$. As *ortho* substituents in the mononitro series the interesting order $CO_2^- < H < COPh < CO_2Me < COMe < CONH_2$ was obtained[2b] and explanations offered. As *ortho* substituents in the dinitro series the same order is obtained, except for the over-all position relative to H, *viz.*, $CO_2^- < COPh < H < CO_2Me < CONH_2$. This corresponds to the operation of the same factors as before, plus a further steric (inhibition) effect due to the additional, though invariant, group (NO_2) in the *ortho* position. This shows up also in the S.I. values, which are some 11–15 times larger in the dinitro series, except for

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[1] To whom inquiries should be made.

[2] (a) J. Miller, THIS JOURNAL, **76**, 448 (1954); (b) J. Miller and V. A. Williams, *ibid.*, **76**, 5482 (1954).

[3] J. Miller, *ibid.*, **77**, 182 (1955).

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TABLE II

2-SUBSTITUENT OF 1-CHLORO-4-NITROBENZENE OR 4-SUBSTITUENT OF 1-CHLORO-2-NITROBENZENE

Substituent	Rate constant at 50°, 10^5k_2, l. mole^{-1} sec.$^{-1}$	Substituent rate factor S.R.F.	Steric index, S.I.	Activation energy (E), cal.	Frequency factor, $\log_{10} B$
2 H	0.847	1	1	24050	11.2
4 H	0.252	1		23650	10.4
2 CHO[a]	241[a]	285[a]	7.86[a]	26500[a]	15.3[a]
4 CHO[a]	564[a]	2240[a]		25200[a]	14.8[a]
2 CN	4940	5830	0.482[a]	17600	10.6
4 CN[a]	706[a]	2810[a]		25700[a]	15.2[a]
4 CONMe$_2$[a]	95.6[a]	380[a]	....	16450[a]	8.1[a]

[a] Values affected by side reaction.

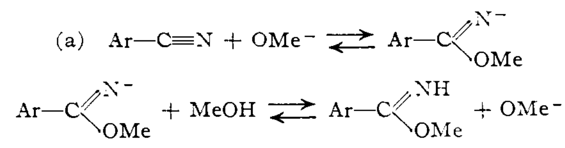
CO_2^- which is about 70 times larger. The exceptionally large value is thought to be due to the larger radius of the effect, being electrostatic in origin. The typical value 11–15 corresponds very well with the ratio obtained by direct comparison of 1-chloro-2,4- and 2,6-dinitrobenzenes, *viz.*, 12. It appears to be unnecessary to recapitulate the explanations offered previously[2b] for the *ortho* effects, except to note two effects of the additional steric factor. In the mononitro series the S.I. for $CONH_2$ was less than 1, indicating an *ortho* acceleration, whereas in the dinitro series the *ortho* group is less activating than the *para*. However the $CONH_2$ is still the most activating *ortho* CO·X group, and with an S.I. much smaller than for any of the others. In the mononitro series the COPh group, though showing a large steric effect in the *ortho* position, was activating compared to H, whereas the additional steric factor in the dinitro series makes it slightly deactivating. The *para* COPh is powerfully activating in both series.

Because of the large size of the $CONMe_2$ group and its inability to attain coplanarity with the ring even when flanked by H atoms, it would be expected that as a compromise conjugation of both the ring and the NMe_2 with the >C=O group would be affected. As regards the resultant effect on $CONMe_2$ as an activating group these two effects act in opposite directions, so that the S.R.F. of the *para* $CONMe_2$ group should not be very different from that of the *para* $CONH_2$ group, as is found experimentally (Table I). However, nucleophilic displacement of the NMe_2 should be facilitated, so that methanolysis in the mononitro series at least (being at a higher temperature than the dinitro series) might involve concurrent displacement of both Cl and NMe_2 by OMe and as a further consequence some displacement of Cl by NMe_2. The abnormally low Arrhenius parameters suggested this and, in view of complexity of the product mixture, the corresponding compound without Cl, *i.e.*, *m*-nitro-N,N-dimethylbenzamide, was exposed to methanolic methoxide in identical conditions to a run with the chloro compound for two half-lives. A mixture of unchanged material and methyl *m*-nitrobenzoate was obtained (confirmed by mixed m.p. with an authentic sample). In contrast the simple amide of the mononitro series gave the pure methoxy compound as product, while *m*-nitrobenzamide did not react at all with methanolic methoxide in the experimental conditions. Results for 4-chloro-3-nitro-N,N-dimethylbenzamide are therefore regarded as approximate only, and the $CONMe_2$ group was investigated in the dinitro series where the side reaction was shown not to occur in the range of kinetic measurements.

In the dinitro series, as already indicated, the $CONMe_2$ group as a *para* substituent was shown to be similar in over-all effect to the $CONH_2$ group. The *ortho* compound had to be investigated in a solvent other than methanol owing to low solubility, and 1/1 methanol–dioxane was chosen. It was necessary then to measure the parent compound (1-chloro-2,4-dinitrobenzene) in the same solvent. There was slight indication of side reaction in the latter stages of runs, especially at the higher temperatures, but the correct product was obtained from the reaction mixture after recrystallization, in more than 70% yield. In complete contrast to the *o*-$CONH_2$ group, the *o*-$CONMe_2$ is actually deactivating, resulting in the large S.I. = 344. In behavior this corresponds to that of the *ortho*-COPh and CO_2^- groups, as do the high values of both E and $\log B$. The unexpectedly high activating power of *o*-$CONH_2$ was regarded[2b] as due to hydrogen bonding (thought incidentally to operate in the transition state). The low activating power of *o*-$CONMe_2$ though consistent with that explanation cannot be regarded as a proof, since the bulk alone of the $CONMe_2$ group could be responsible for the difference.

The solvent ratio 1:1 (v./v.) methanol–dioxane to methanol = 3.28 at 0° is consistent with the Hughes–Ingold theory of solvent action,[7] and corresponds to the almost identical ratio obtained by Briner and Miller[8] for reaction of the same compound (1-chloro-2,4-dinitrobenzene) in 1:1 (v./v.) methanol–methyl acetate and methanol.

The *o*-CHO group shows the same anomalous Arrhenius parameters (high E and $\log B$) and activating power (unexpectedly low) already demonstrated for *para* CHO and CN,[2a] whereas the *o*-CN appears to be quite normal in these respects—values being very close to those for the *o*-NO_2 group.[5,6] The explanation given originally[2a] for the anomalies with para CHO and CN was either some unusual electronic effect or reversible side-reactions not affecting the products and kinetic form[9]—appropriate and well known side-reactions being hemiacetal and imido ester formation, respectively.[10–15] Thus



$$\text{(a)}\quad Ar{-}C{\equiv}N + OMe^- \rightleftarrows Ar{-}C{\overset{\displaystyle N^-}{\underset{\displaystyle OMe}{\lessgtr}}}$$

$$Ar{-}C(=N^-){-}OMe + MeOH \rightleftarrows Ar{-}C(=NH){-}OMe + OMe^-$$

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[7] E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 252 (1935).

[8] G. P. Briner and J. Miller, *ibid.*, 4682 (1954).

[9] It was pointed out by a referee to that paper that the kinetic form could be unaffected by such reactions, the observed result being abnormal Arrhenius parameters and low S.R.F.'s.

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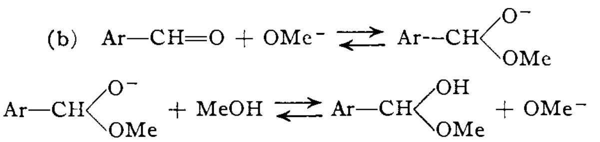

$$\text{(b)}\quad \mathrm{Ar{-}CH{=}O + OMe^- \rightleftharpoons Ar{-}CH}\begin{array}{l}\mathrm{O^-}\\ \mathrm{OMe}\end{array}$$

$$\mathrm{Ar{-}CH}\begin{array}{l}\mathrm{O^-}\\ \mathrm{OMe}\end{array} + \mathrm{MeOH} \rightleftharpoons \mathrm{Ar{-}CH}\begin{array}{l}\mathrm{OH}\\ \mathrm{OMe}\end{array} + \mathrm{OMe^-}$$

A CHO group *ortho* to Cl is expected to be forced out of the plane of the ring, and hemiacetal formation therefore becomes possible without series interference due to further loss of conjugation. However, a CN group *ortho* to Cl can be coplanar, while the imido ester cannot. Loss of conjugation if the latter were formed should thus hinder or prevent its formation. With the higher base rate of the 1-chloro-4-nitro as against the 1-chloro-2-nitro series in Cl replacement, the observed result with the *o*-CN compound is that methanolysis of Cl occurs without accompanying imido ester formation. In order to confirm the above reasonable argument, an infrared investigation[4] of the two nitriles, together with *m*-nitrobenzonitrile and benzonitrile, was chosen as the first paper in a separate series of investigations of interactions between nucleophilic reagents and CN and CO·X groups. The relevant results from that paper which used conditions as close as possible to those of kinetic experiments, are that with methanolic methoxide 4-chloro-3-nitrobenzonitrile and *m*-nitrobenzonitrile formed imido ester to the extent of about 80% of the amount originally present, while 2-chloro-5-nitrobenzonitrile as well as benzonitrile formed no detectable amounts of imido ester. The same results would be expected by analogy with those determined in references 10–12, so that the true S.R.F. of the *p*-CN may be estimated as not less than 10^4. It is intended to investigate these compounds also in connection with other work proceeding on reagents in aromatic Sn reactions, and it is hoped that a reagent will be found which will replace halogen conveniently without the concurrent interaction with CHO and CN groups. Owing to experimental difficulties it was impossible to carry out infrared investigations on the CHO compounds as was done with the nitriles, but in view of the well known correspondence of hemiacetal and imido ester formation, the experimental evidence for the latter is regarded as support for the former.

Experimental

Rate constants were obtained graphically after stopping reaction with standard dilute acid, and estimating base or chloride ion potentiometrically. Values of k_2 were always determined at not less than three temperatures (typical range 20–40°), and with one exception a minimum of six separately determined values of k_2 were used in determining E and thus log B by a least squares analysis of corresponding values of $\log_{10} k_2$ and reciprocal temperature. The "probable errors" so obtained were less than the estimated normal error of ±300 cal. in E and ±0.25 in log B. For a fast reacting compound measured over a short temperature range, errors up to about 1 kcal. in E and 1 in log B are possible.

The expected product methoxy compounds were isolated from reaction mixtures except for 4-chloro-3-nitro-N,N-dimethylbenzamide (see Discussion).

Preparation of Materials and Experimental Rate Constants. **2-Chloro-3,5-dinitrobenzamide.**—This was prepared from the acid *via* the acid chloride by ammonolysis with aqueous ammonia.[16] The over-all yield of product, recrystallized from water, was 20%, with m.p. 179°, lit.[17] 180°); rate constants ($10^6\,k_2$): 3170 (−4.8°), 5580 (0°) and 9810, 9810 (4.95°).

2-Chloro-3,5-dinitro-N,N-dimethylbenzamide.—Using minimum quantities of dry solvent, the acid chloride in acetone was treated at 0° with 2 moles of dimethylamine in acetone added slowly with stirring. The product crystallized out. After recrystallization from MeOH, 46% over-all yield of material, m.p. 195°, was obtained. With the acid which has a similar m.p., a 20° depression of mixed m.p. was obtained. Dilution of the reaction mixture gave oily products which were not investigated. *Anal.* Calcd. for $C_9H_8N_3O_5Cl$: C, 39.50; H, 2.95; N, 15.36; O, 29.24. Found: C, 40.13; H, 3.17; N, 15.19; O, 28.92. Rate constants ($10^5\,k_2$): 125, $125._5$ (0.1°); 1090, 1100 (16.8°); 2930, 2950 (25.5°). The product had m.p. 107.5°. *Anal.* Calcd. for $C_{10}H_{11}N_3O_6$: C, 44.61; H, 4.12; N, 15.61; O, 35.66. Found: C, 44.78; H, 3.85; N, 15.93; O, 35.4.

2-Chloro-3,5-dinitrobenzophenone.—This was prepared from the acid chloride by a Friedel–Crafts reaction.[18] After recrystallization from glacial acetic acid then methanol a 50% over-all yield of product was obtained with m.p. 150.5° (lit.[18] 149°); rate constants ($10^5\,k_2$): 468, 468 (12.0°); 1070, 1075 (20.0°); 4530, 4570 (35.0°).

2-Chloro-5-nitrobenzaldehyde.—This was prepared in 46% yield by the nitration of *o*-chlorobenzaldehyde[19] and recrystallization from aqueous acetic acid to give a product, m.p. 78° (lit.[19] 78–79°); rate constants ($10^5\,k_2$): 136, 137 (45.6°); 824, 836 (60.0°), 9740, 9850 (81.9°).

2-Chloro-5-nitrobenzonitrile.—Absolute HNO_3 was used to nitrate[20,21] *o*-chlorobenzonitrile, prepared from *o*-chloroaniline by a Sandmeyer reaction. After recrystallization from methanol, a 28% over-all yield of product, m.p. 107°, was obtained. Further recrystallization raised the m.p. to 108–109° (lit.[20] 108–109°); rate constants[21] ($10^6\,k_2$): 495 (25.0°), 823, 826 (30.25°); 1290, 1300 (35.0°): 131_5 (35.1°); 3300 (45.3°); 3310 (45.35°).

4-Chloro-3-nitro-N,N-dimethylbenzamide.—This was prepared from the acid[2a] *via* the acid chloride, which was reacted with 2 moles of dimethylamine in acetone. After dilution with water, the product was obtained in 78% yield, and after recrystallization from MeOH had m.p. 110° (lit.[22] 113.5°). Owing to the difference of 3.5° from the lit. m.p. this compound was analyzed. *Anal.* Calcd. for $C_9H_9N_2O_3Cl$: C, 47.30; H, 3.97; Cl, 15.5. Found: C, 47.23; H, 3.90; Cl, 15.4. Rate constants ($10^5\,k_2$): 67.1, 67.4 (45.5°); 90.4 (49.1°); 208, 208 (60.2°); 968, 973 (82.0°).

4-Chloro-3,5-dinitro-N,N-dimethylbenzamide.—This was prepared analogously to the 2-chloro compound, except that the reaction mixture was diluted with water, washed with cold 1:1 H_2SO_4–H_2O, then with cold water. Repeated recrystallization from MeOH gave 71% yield of product m.p. 140.5°. *Anal.* Calcd. for $C_9H_8N_3O_5Cl$: C, 39.50; H, 2.96. Found: C, 39.82; H, 3.23. Rate constants ($10^5\,k_2$): 327 (0.2°); 895 (10.0°); 1830 (17.0°); 1980 (18.1°); 3050 (22.9°); 3350 (23.9°). The product had m.p. 116.5°. *Anal.* Calcd. for $C_{10}H_{11}N_3O_6$: C, 44.61; H, 4.12; O, 35.66. Found: C, 44.86; H, 4.19; O, 35.40.

1-Chloro-2,4-dinitrobenzene.—See reference 5.

Solvents.—Methanol was prepared as in previous papers. Dioxane was purified by successive treatments with dil. HCl, solid KOH and Na,[23] and the fraction boiling between 101–102° collected.

Analyses were by Dr. K. W. Zimmerman of Melbourne, Australia; m.p.'s are corrected.

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