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THE RELATIVE REACTIVITY OF FLUORO- AND CHLORO-2,4-DINITROBENZENES IN THEIR REACTIONS WITH AMINES. A RE-INVESTIGATION.

Francesco Pietra and Francesco Del Cima,
Istituto di Chimica Generale, Università di Pisa,
Pisa, Italy.

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Recently we reported data concerning the reactivities of fluoro-2,4-dinitrobenzene (FDNB) or chloro-2,4-dinitrobenzene (CDNB) with piperidine (1), 2-methylpiperidine and cis-2,6-dimethylpiperidine in benzene (2). Further research has shown that the data relative to the reactions of cis-2,6-dimethylpiperidine were in error due to the presence of very reactive impurities in the amine used. This was a commercial sample of 2,6-dimethylpiperidine (b.p. 126-9°C). Its hydrochloride had been twice recrystallized from ethanol (3b, 4, 5) [m.p. 288-289°C, uncorrected; lit. 289-91°C (3b), 280-2°C (6), 287°C (7)], the amine set free with potassium carbonate, refluxed over potassium hydroxide then over sodium and distilled [b.p. 127-128°C; lit. 126-127°C (3b)].

Cis- and trans-2,6-dimethylpiperidine have now been obtained by Ladenburg reduction of 2,6-dimethylpyridine (4) followed by careful fractionation.[x] V.p.c.[xx] shows no contami-

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[x] Fractionation at 73 Torrs under nitrogen through a column 3 ft. x 3/5 in. packed with Fenske glass helices 1/10 in. diameter.

[xx] Column 6 ft. x 1/8 in. 1-hydroxyethyl 2-heptadecenyl glyoxalidine on 60/80 mesh KOH-washed Chromosorb W; temp. 90°C; flame ionization detector; flow rate, N_2, 25 ml/min.

nation in *cis*-2,6-dimethylpiperidine, whereas *trans*-2,6-dimethylpiperidine contains about 0.6% of the *cis* isomer. The higher boiling isomer has been reported to have the *trans* configuration (3).

We report here new kinetic data for the reaction of CDNB with *cis*-2,6-dimethylpiperidine in benzene and for the reactions of CDNB or FDNB with *trans*-2,6-dimethylpiperidine in benzene. These data show that the *trans* isomer is not much more reactive than the *cis* one toward CDNB and allow the reactivity ratio ArF/ArCl to be evaluated in a greater reactivity range than that spanned by piperidine and 2-methylpiperidine (2).

Rate data for the reactions of CDNB are collected in Table I. The second-order rate coefficient appears to be very little dependent on amine concentration in the reaction with either *cis*- or *trans*-2,6-dimethylpiperidine.[*] Extrapolation to 25°C gives 6.3×10^{-8} and 4.0×10^{-7} mole^{-1} l. sec.^{-1} for the reactions of *cis*- and *trans*-2,6-dimethylpiperidine, respectively.

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[*] Good first- or second-order plots were obtained up to 90% reaction completion for experiments carried out under nitrogen. Formation of N-2,4-dinitrophenyl-*cis*-2,6-dimethylpiperidine, m.p. 84-84.5°C, or N-2,4-dinitrophenyl-*trans*-2,6-dimethylpiperidine, m.p. 69-70°C (m.p. uncorrected), is quantitative. Structural assignments of these two compounds were made by PMR spectroscopy. The aromatic protons in *meta* position to the nitrogen of the *cis* compound in a 10% solution in CCl_4 have the same chemical shift as shown by decoupling experiment at 100 MC. However, a solution of the *cis* compound in benzene-*d*$_6$ gives a tipical ABX spectrum which can be ascribed to the aromatic part.[**]

[**] Thanks are due to Dr. A. Melera, Varian AG Zürich, for the spectrum in benzene, decoupling experiment and the interpretation thereof.

TABLE I

Second-order rate coefficients, *k*, for the reactions of chloro-2,4-dinitrobenzene[a] (CDNB) with *cis*- or *trans*-2,6-dimethylpiperidine in benzene.

cis-2,6-dimethylpiperidine *M*	temp. °C	$10^6 \times k$ mole^{-1} l. sec.$^{-1}$
0.101	100.4	8.91
0.801	100.4	10.1
0.101	89.9	4.95
0.801	89.9	5.92
0.101	80.1	2.73
0.801	80.1	3.32
trans-2,6-dimethylpiperidine *M*		
0.109	100.4	40.0
0.650	100.4	40.7
0.650	80.1	14.2
0.650	60.0	4.45

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[a] Initial concentration of CDNB 0.050 *M*. Experiments in benzene at initial concentration of CDNB 0.0050 *M* show that within the range 0.0050 - 0.050 *M* the reaction order with respect to CDNB is unity.

Brady and Cropper reported (5) a rate coefficient of about 7 x 10^{-5} mole^{-1} l. sec.^{-1} for the reaction of CDNB with 2,6-dimethylpiperidine in ethanol at 25°C (the configuration of the amine was not established but from the boiling point reported, 127°C, it would now appear (3) to consist mainly of the cis isomer). As the solvent effect from benzene to ethanol is expected to be small for this reaction and in the direction of decreasing rate (8), our data show that the rate reported by Brady and Cropper (5) can not be referred to chloride displacement by either cis- or trans-2,6-dimethylpiperidine. Apparently, as already suspected by Bunnett and Zahler (9), Brady and Cropper may have actually measured displacement by ethoxide ions.

The kinetic data for the reaction of FDNB with trans-2,6-dimethylpiperidine in benzene are listed in Table II.* In this case there is a definite although not very pronounced increase in the second-order rate coefficient with increasing amine concentration. The trend at 60°C parallels that at 100°C so that it is reasonable to assume a similar trend also at 25°C. The second-order rate coefficient thus extrapolated to 25°C and zero amine concentration is 1.0 x 10^{-5} mole^{-1} l. sec.^{-1}.

As far as the reaction of FDNB with cis-2,6-dimethylpiperidine in benzene is concerned, preliminary results (100°C; FDNB 0.06 M; cis-2,6-dimethylpiperidine 0.8 M; experiment carried out under nitrogen) show that only about 70% of

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* Formation of N-2,4-dinitrophenyl-trans-2,6-dimethylpiperidine is quantitative in experiments carried out under nitrogen. The second-order rate coefficient increases – though not greatly – with the percentage reaction. The second-order rate coefficients were computed from initial rates.

Table II

Second-order rate coefficients, *k*, for the reaction of fluoro-2,4-dinitrobenzene[a] (FDNB) with *trans*-2,6-dimethylpiperidine in benzene.

trans-2,6-dimethyl-piperidine *M*	temp. °C	$10^5 \times k$[b] $mole^{-1} l. sec.^{-1}$
0.0504	100.4	18.1
0.125	100.4	19.0
0.252	100.4	23.0
0.0504	80.1	8.98
0.0504	60.0	4.74
0.184	60.0	7.15

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[a] Initial concentration of FDNB 0.025 *M*. Experiments in benzene at initial concentration of FDNB 0.0048 *M* show that within the range 0.0048 - 0.025 *M* the reaction order with respect to FDNB — computed from initial rates — is about unity.

[b] Initial rates. Average values of two runs.

N-2,4-dinitrophenyl-cis-2,6-dimethylpiperidine is formed (I.R. analysis). The competing reaction(s) is (are) as yet unidentified. The second-order rate coefficient based on the formation of the arylamine has comparable magnitude with that obtained for the corresponding reaction of CDNB at 100°C.

We are now in the position of comparing the relative leaving group ability of fluoride and chloride in a ''slow'' solvent like benzene and in a reactivity range of closely related nucleophiles of about 200 thousand-fold from piperidine to trans-2,6-dimethylpiperidine. Comparing the second-order rate coefficient for a particular reaction of CDNB with the uncatalyzed second-order rate coefficient for the corresponding reaction of FDNB (2), we obtain ArF/ArCl = 7, 35 and about 25 for piperidine, 2-methylpiperidine and trans-2,6-dimethylpiperidine, respectively.

Thus the previous statement that the relative reactivity ArF/ArCl is not greatly dependent on the steric bulk of the reacting amine (2), while must be referred to a set of amines ranging from piperidine to trans-2,6-dimethylpiperidine, is still valid and in a reactivity range much greater (200,000) than it was previously supposed (2).

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