compared to the free energy of the unhindered *para* transition state. This large increase will overwhelm the (assumed) slightly elevated free energy of the *o*-nitrophenyl halide, causing the *ortho* isomer to react more slowly. This is a powerful effect which more than overcomes the inherent tendency of the nitro group for preferential *ortho* activation. Experimentally, this situation is evident in the reactions of nitrophenyl halides and dinitrobenzenes with alkoxide and thiophenoxide ions; with one exception, all go faster in the *para* series. The exception concerns the reactions of *o*- and *p*-fluoronitrobenzene with sodium ethoxide[22]; in this case, steric interference with coplanarity is small because of the small size of the fluorine atom, and the inherent preferentially *ortho*-activating effect of the nitro group still prevails.[44]

When the reagent is an anion, another effect which no doubt has a bearing on *ortho:para* ratio is electrostatic repulsion in the transition state between the negatively charged oxygen atoms of the nitro group and the still partially negatively charged incoming group.[7] This influence opposes *ortho* substitution, and tends to decrease the *ortho*: *para* ratio. It is not a major effect, for if it were, 2,4-dichloronitrobenzene would undergo considerable replacement of the 4-chlorine by anion reagents. Speaking of 2,4-dichloronitrobenzene, it should be noted that its nitro group is *always* bounded by an *ortho* substituent, and will be sterically hindered in both the *ortho* and *para* transition states; hence our statement that it approaches the situation of "all other things being equal."

In the reactions of *o*- and *p*-nitrophenyl halides with amines, the favorable electrostatic interactions ("built-in solvation") in the *ortho* transition state once more swing the delicate balance of factors back to favoring *ortho* substitution. Here we have an overlay of three effects: first, the inherent preferentially *ortho*-activating effect of the nitro group; second, steric interference with coplanarity in the *ortho* transition state, tending to retard *ortho* substitution; and finally, "built-in solvation" in the *ortho* transition state which restores the predominance of *ortho* substitution.

In the following paper, it is shown that "built-in solvation" plays an important part in determining the *ortho: para* ratio in activation by the carboxylate ($-COO^-$) group.

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(44) It is interesting, however, that *p*-fluoronitrobenzene reacts slightly faster with sodium *methoxide*.[21]

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NORTH CAROLINA]

The *ortho: para* Ratio in Activation of Aromatic Nucleophilic Substitution by the Carboxylate Group

BY J. F. BUNNETT, R. J. MORATH AND T. OKAMOTO[1]

RECEIVED APRIL 9, 1955

The carboxylate group ($-COO^-$) is mildly *para* activating for aromatic nucleophilic substitution. It is *ortho* deactivating for displacement of chlorine by methoxide ion but rather strongly *ortho* activating for displacement of chlorine by piperidine. The *ortho*-activating effect arises from an increase in the entropy of activation. This phenomenon is to be understood as a consequence of "built-in solvation" in the transition state, which decreases the need for participation of solvent molecules in the transition complex.

In the preceding paper[2] we have interpreted successfully the high *ortho: para* rate ratio in the reactions of chloronitrobenzenes with amines, in contrast to the low *ortho:para* ratio in reactions with alkoxides, in terms of a favorable electrostatic interaction between oppositely charged atoms in the transition state of the *o*-aminodechlorination[3] reactions. It is reasonable to expect that such electrostatic interaction should have an important effect on the rates of other reactions. We now report experiments showing the carboxylate[4] group to exert a large activating effect on *o*-piperidinodechlorination.[3] This result also is to be understood in terms of favorable electrostatic interactions in the transition state.

For some time the carboxylate group has been recognized[5-7] as mildly activating toward aromatic nucleophilic substitution in the *para* position. Recently, Miller and Williams[7] showed that the carboxylate group is definitely *deactivating* toward *o*-methoxydechlorination. The contrast between their discovery and ours is striking.

We have determined rate coefficients for the reactions of sodium 4-chloro-3-nitrobenzoate (I) and of sodium 2-chloro-5-nitrobenzoate (II) with piperi-

(1) On leave from the Pharmaceutical Institute, University of Tokyo.

(2) J. F. Bunnett and R. J. Morath, THIS JOURNAL, **77**, 5051 (1955).

(3) This is a systematic name for a substitution reaction. Such names are composed of the parts: the name of the incoming group, the syllable "de," the name of the departing group, and the suffix "ation"; *cf.* J. F. Bunnett, *Chem. Eng. News*, **32**, 4019 (1954); *J. Chem. Soc.*, 4717 (1954).

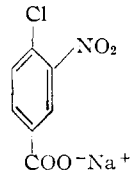
(4) The group $-COO^-$, resulting from the removal of a proton from a carboxyl group, has variously been called the "carboxylate ion" or the "carboxylate" group, though authors have frequently avoided such names by using the formula of the group instead. We advocate the name, *carboxylate* group, as being simple, sufficient and definite. Analogously, we shall call $-SO_3^-$, resulting from removal of a proton from a sulfo group, the *sulfonate* group.

(5) (a) H. Rouche, *Bull. Acad. roy. Belg., Classe des sciences*, [5] **7**, 534 (1921); *Chem. Zentr.*, **93**, I, 22 (1922). (b) E. Berliner and L. C. Monack, THIS JOURNAL, **74**, 1574 (1952).

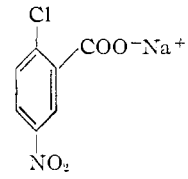
(6) J. F. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 313 (1951).

(7) J. Miller and V. A. Williams, *J. Chem. Soc.*, 1475 (1953).

dine in 93% ethanol solution. The reaction rates were followed by a spectrophotometric technique similar to that of the preceding paper.[2]



I



II

Our results are summarized in Table I. The gist of Miller and Williams' results,[8] as they pertain to the effect of the carboxylate group, is presented in Table II.

TABLE I

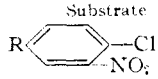
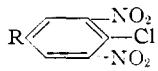
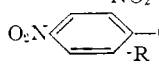
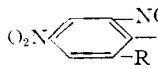
THE EFFECT OF THE CARBOXYLATE GROUP ON *o*- AND *p*-PIPERIDINODECHLORINATION[a]

	R = H[b]	R = COO⁻	R = H[b]	R = COO⁻
k at 102.0°, l. mole^{-1} min.$^{-1}$ × 10^3	4.02	14.1	1.72	56.9
ΔE, kcal.	17.7	18.1	15.2	17.3
$\Delta S^{\mp}$, e.u.	−33	−29	−41	−29
k_{COO^-}/k_H		3.5		33.0

[a] Reagent: piperidine in 93% ethanol. [b] Data from ref. 2.

TABLE II

THE EFFECT OF THE CARBOXYLATE GROUP ON *ortho*- AND *para*-METHOXYDECHLORINATION[a,b]

Substrate	Rate coefficient at 50.0°, l. mole^{-1} min.$^{-1}$ R = H	R = COO⁻	k_{COO^-}/k_H
	1.6×10^{-4}	11.8×10^{-4}	7.5
	0.62	2.8	4.5
	5.4×10^{-4}	1.9×10^{-4}	0.35
	17.2	0.45	0.03

[a] Reagent: sodium methoxide in methanol. Data from ref. 7.

It should be noted that the *p*-carboxylate group exerts a mild activating effect on reactions both with sodium methoxide and with piperidine. However, whereas the *o*-carboxylate group is distinctly *deactivating* for methoxydechlorination, it is distinctly *activating* for piperidinodechlorination. Miller and Williams have ascribed the *deactivating* effect to electrostatic repulsion, in the transition state, between negatively charged carboxylate oxygen atoms and the negatively charged methoxide oxygen atom. We concur. We ascribe the *activating* effect to favorable electrostatic interaction, in the transition state, between the negative charge on the carboxylate oxygen atoms and the developing positive charge on the piperidine nitrogen atom. As before,[2] we cannot say to what extent this interaction may involve the piperidine hydrogen atom in hydrogen bonding.

The thermodynamic data in Table I show that the *o*-carboxylate group increases the rate by increasing the entropy of activation. Indeed, the increase in the entropy of activation is so great that the rate increases 33-fold in spite of a significant increase in the energy of activation. This pattern, of an increase in energy of activation more than offset by an increase in entropy of activation, is a typical consequence of a lesser increase in solvation during formation of the transition state.[11] This leads us to believe that the activating effect of the *o*-carboxylate group on piperidinodechlorination arises from electrostatic interaction, between negatively charged carboxylate oxygen atoms and the positively charged piperidine nitrogen atom, which acts as a kind of mutual solvation of these electrical poles ("built-in solvation") and decreases the requirement for participation of solvent molecules in the transition state.[12]

The over-all *ortho:para* ratio associated with the effect of the carboxylate group on nucleophilic substitution may, it thus appears, be described as less than 1.0 when the reagent is an anion and greater than 1.0 when the reagent is a neutral molecule which develops a positive charge in the transition state. This variation in *ortho:para* ratio bears some resemblance to the variable effect of the nitro group,[2] but the analogy is limited to similar electrostatic interactions in the transition states for *ortho* substitution. Strong inductive and mesomeric effects, the latter sensitive to steric influences, play a major role in determining the activation pattern by the nitro group but only a minor part in the case of the carboxylate group. The difference in the effects of the two groups is illustrated by the fact[13] that sodium methoxide displaces principally the 4-chlorine from sodium 2,4-dichlorobenzoate, but principally the 2-chlorine from 2,4-dichloronitrobenzene.[2]

Activation in Copper-catalyzed Reactions.—Goldberg[14] has pointed out that the carboxylate group exerts a powerful and specific *ortho*-activating effect in the Ullmann copper-catalyzed condensation of aryl halides with nucleophilic reagents. Extending a suggestion of Bunnett and Zahler,[15] Goldberg has postulated that a cuprous ion coördinates with the halogen atom and with an oxygen atom of an *o*-carboxylate group to form a chelate ring system in which the halogen atom is particularly susceptible to being displaced by nucleophilic reagents.

(8) We have doubts[9] about the absolute accuracy of the rate coefficients reported by Miller and Williams. We are, however, inclined to agree with Miller[10] that conclusions based on comparisons amongst their data are probably valid. Since energy and entropy of activation values are particularly sensitive to errors in rate coefficients, we shall not consider Miller and Williams' Arrhenius parameters, some of which have extraordinary values.

(9) J. F. Bunnett, H. Moe and D. Knutson, THIS JOURNAL, **76**, 3936 (1954).

(10) J. Miller, *Chemistry & Industry*, 1428 (1954).

(11) A. F. Chadwick and E. Pacsu, THIS JOURNAL, **65**, 392 (1943). S. Winstein and H. Marshall, *ibid.*, **74**, 1120 (1952).

(12) Surely the nitro group carries considerable negative charge in the transition state from II and piperidine, and must require solvation This requirement is probably largely offset, however, by an actual *decrease* in solvation of the carboxylate group as the transition state is formed.

(13) L. M. F. van de Lande, *Rec. trav. chim.*, **51**, 98 (1932).

(14) A. A. Goldberg, *J. Chem. Soc.*, 4368 (1952).

(15) Reference 6, p. 394.

This suggestion makes sense. It should be noted, though, that Goldberg's chelate ring with its principally covalent bonds is rather different from the electrostatic interactions ("built-in solvation") which we have proposed in this and the preceding paper.

Experimental

Materials.—4-Chloro-3-nitrobenzoic acid and 2-chloro-5-nitrobenzoic acid were prepared by nitration of, respectively, *p*- and *o*-chlorobenzoic acid. Each of the chloronitrobenzoic acids was allowed to react with piperidine (by dissolving the acid in excess piperidine and warming to reflux for about two minutes). The products, recrystallized from 95% ethanol, were 3-nitro-4-piperidinobenzoic acid, m.p. 207–208° (lit.[16] 202–203°), and 5-nitro-2-piperidinobenzoic acid, m.p. 199–200° (lit.[16] 201–202°). These authentic products were used in preparing solutions of the composition expected at the completion of reaction in the kinetic runs. Such solutions are useful in standardizing the analytical procedure. These nitropiperidinobenzoic acids also were isolated in high yield from reactions of piperidine with the corresponding chloronitrobenzoic acids under the conditions of the rate studies.

Piperidine and 93% ethanol for the rate studies were prepared as previously described.[2]

Rate Measurements.—The spectrophotometric technique previously described[2] was used. Piperidine and the two chloronitrobenzoic acids have negligible absorption in the visible range while the nitropiperidinobenzoic acids absorb strongly. 3-Nitro-4-piperidinobenzoic acid was determined by optical density measurements at 415 mμ, and 5-nitro-2-piperidinobenzoic acid by measurements at 390 mμ.

Our first runs were set up so as to provide second-order kinetics, the initial concentration of the sodium chloronitrobenzoate being about 0.015 *M* and that of the piperidine about 0.03 *M*. However, plots of $1/(a - x)$ *vs.* t (valid if the stoichiometry is: $ArCl + 2R_2NH \rightarrow ArNR_2 + R_2NH_2Cl$) showed an upward curvature, while plots of an appropriate log term *vs.* t (valid if the stoichiometry is: $C_6H_3NO_2ClCOO^- + R_2NH \rightarrow C_6H_3NO_2NR_2COOH + Cl^-$) showed a downward curvature. This indicated intermediate stoichiometry, not unreasonable considering that the basicity of an amine decreases while that of an acylate ion increases as the solvent changes from water to 93% ethanol.

Our principal runs were set up with piperidine in 40-fold excess, the initial concentrations being about 0.06 *M* (for piperidine) and 1.5×10^{-3} *M* (for the sodium chloronitrobenzoate). These runs provided clean-cut first-order kinetics. The first-order rate coefficients were divided by the piperidine concentration (in the reacting solution), and thus converted to second-order rate coefficients. As a check on this conversion, we determined the first-order rate coefficient for the reaction of piperidine with *o*-chloronitrobenzene in 93% ethanol, and then converted it to a second-order rate coefficient. The resulting value, 3.52×10^{-3} l. mole^{-1} min.$^{-1}$ at 101.8°, compares with Bunnett and Morath's[2] 3.88×10^{-3} l. mole^{-1} min.$^{-1}$ at 101.5°.

Infinity optical densities for a run with sodium 4-chloro-3-nitrobenzoate (I) at 119.3° and for a run with sodium 2-chloro-5-nitrobenzoate (II) at 101.8° were within 1% of the theoretical value for 100% conversion to the corresponding nitropiperidinobenzoic acids. This shows that no significant side reactions took place.

Since the reaction of II with piperidine at 46.0° was moderately slow, some quenched samples of the reaction solution had to stand for days before they could be analyzed as a group with other samples from the same run. A slight drift in optical density was observed to occur. It was established that 5-nitro-2-piperidinobenzoic acid undergoes some esterification under the conditions existing in the quenched solution. A small amount of the ethyl ester was isolated, by chromatography, and was identified by comparison of its infrared spectrum with that of an authentic sample. This complication was avoided, in later runs, by chilling the ampoules removed from the thermostat and storing them in a "deep freeze" until the run was completed, at which time they were all opened, quenched in the usual way, and analyzed directly.

Following are the second-order rate coefficients we determined, in units of l. mole^{-1} min.$^{-1}$. Each is the average value from two to four supposedly identical runs. The average deviation was about 2.5% for runs with I and less than 1% for runs with II.

Sodium 4-chloro-3-nitrobenzoate (I) at 101.8°, 1.39×10^{-2}; at 119.3°, 4.12×10^{-2}.

Sodium 2-chloro-5-nitrobenzoate (II): at 101.8°, 5.63×10^{-2}; at 46.0°, 9.62×10^{-4}.

Arrhenius activation energies and entropies of activation were calculated from standard expressions. ΔE values are uncertain by about ±1.0 kcal. in the case of I and by about ±0.1 kcal. in the case of II. The uncertainty in $\Delta S^{\ddagger}$ values is about ±3.0 cal./deg. in the case of I and about ±0.2 cal./deg. in the case of II.

Acknowledgments.—We thank the Office of Ordnance Research, U. S. Army, for financial assistance. A Fulbright travel grant to one of us is also appreciated.

CHAPEL HILL, N. C.

(16) R. J. W. Le Fevre and E. E. Turner, *J. Chem. Soc.*, 1113 (1927).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WYOMING]

The *para*-Claisen Rearrangement. III. Kinetics of the Rearrangement of Some γ-Substituted Allyl Ethers of Methyl *o*-Cresotinate[1]

BY SARA JANE RHOADS AND ROBERT L. CRECELIUS[2]

RECEIVED APRIL 14, 1955

Rates of rearrangement of the allyl (Ia), the γ-methylallyl (Ib), and the γ-ethylallyl (Ic) ethers of methyl *o*-cresotinate have been measured at several temperatures. Activation energies and entropies have been calculated and are discussed in terms of the structures of the compounds and the mechanism of the rearrangement.

The kinetics of the *para*-Claisen rearrangement of the allyl ether of 2,6-dimethylphenol have been studied by Tarbell and Kincaid[3] and constitute the only detailed kinetic examination of this rearrangement reported to date.[4] It seemed desirable to collect more rate data on this rearrangement and especially to extend such studies to a series of substituted allylic ethers in which the γ-substituent was systematically varied. This paper reports the results of such an investigation.

Rates of rearrangement in the pure liquid have been measured for the allyl (Ia), the γ-methylallyl (Ib) and the γ-ethylallyl (Ic) ethers of methyl *o*-cresotinate. The reactions were followed by the change in refractive index and showed good first-order rate dependence up to 80–90% completion.

(1) Taken from the Ph.D. dissertation of R. L. Crecelius, University of Wyoming, June, 1954.

(2) Research Corporation Fellow, 1952–1953.

(3) D. S. Tarbell and J. F. Kincaid, THIS JOURNAL, **62**, 728 (1940).

(4) H. Schmid and K. Schmid, *Helv. Chim. Acta*, **36**, 489 (1953), report rate data for the allyl ether of methyl *o*-cresotinate at one temperature. Their value of $k_1 = 2.62 \times 10^{-1}$ sec.$^{-1}$ at 167.7° agrees well with ours (Table I).