[6] *Sandoz AG.*, S.P. 455 083 (1966); *V. Chmàtal & Z. J. Allan*, Coll. czechosl. chem. Commun. *30*, 1205 (1965).
[7] *S. M. Neale & W. A. Stringfellow*, J. Soc. Dyers Colourists *59*, 241 (1943).
[8] *J. A. Rupley*, J. physic. Chemistry *68*, 2002 (1964); *D. Wagner*, Textil-Praxis *1969*, 310, 383.
[9] *W. Brunning & A. Holtzer*, J. Amer. chem. Soc. *82*, 4865 (1961); *M. J. Schick*, J. physic. Chemistry *68*, 3585 (1964).
[10] *M. Abu-Hamdiyyah*, J. physic. Chemistry *69*, 2720 (1965); *G. Némethy*, Angew. Chem. *79*, 260 (1967).
[11] *I. M. Klotz & V. H. Stryker*, J. Amer. chem. Soc. *82*, 5196 (1960); *G. C. Kresheh & L. Benjamin*, J. physic. Chemistry *68*, 2476 (1964).
[12] *A. Katayama, I. Matsuura, K. Konshi & N. Kuroki*, Kolloid-Z. *202*, 157 (1965); *P. Mukerjee & A. K. Ghosh*, J. physic. Chemistry *67*, 193 (1963).
[13] *H. Zollinger*, Helv. *38*, 1617 (1955).
[14] *J. R. Penton & H. Zollinger*, Helv. *54*, 573 (1971).
[15] *C. D. Ritchie & D. J. Wright*, J. Amer. chem. Soc. *93* (1971), im Druck; Vortrag *C. D. Ritchie*, Réunion Annuelle de la Société de Chimie Physique, Paris 1970.
[16] *T. Gast*, in Landolt-Börnstein, «Zahlenwerte und Funktionen», Bd. II/6, S. 742f., Springer, Berlin 1959.
[17] *W. J. Dunning & W. J. Shutt*, Trans. Farad. Soc. *34*, 169 (1922).
[18] *P. S. Albright*, J. Amer. chem. Soc. *59*, 2100 (1937).
[19] *E. J. Koller & H. Zollinger*, Helv. *39*, 1610 (1956).

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58. The Rôle of Solvent Participation in Electrophilic Aromatic Substitution: Rates of a Diazo Coupling Reaction in Water and in Aprotic Polar Solvents

24th communication on diazo coupling reactions[1])

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(13. I. 71)

Summary. The rates of the diazo coupling reaction of 4-toluenediazonium salts with N,N-dimethylaniline in tetramethylene sulfone, acetonitrile, water, and nitromethane at 30 °C are the same within a factor of 5. No significant influence of 'gegenions' ($HSO_4^\ominus$ or $BF_4^\ominus$) was found. The results are explained by postulating little solvent reorganisation in the transition state. They are discussed comparatively with solvent effects in other electrophilic aromatic substitutions, particularly with regard to the reactions of nitronium salts.

Ten years ago, *Olah et al.* [2] observed that the nitration of aromatic hydrocarbons in tetramethylene sulfone (sulfolane) proceeded at a much faster rate when nitronium salts were used as nitrating agents in place of conventional nitrating agents. Similar results were obtained for other electrophilic aromatic substitutions, *e.g. Friedel-Crafts* reactions.

These results were surprising in view of the fact that *Ingold, Hughes* and their coworkers [3] had demonstrated beyond all doubt that under conventional conditions, *e.g.* in nitric acid/sulfuric acid mixtures, it is the nitronium ion which attacks the substrate (*e.g.* benzene). Therefore it seemed that the change to another (more

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[1]) 23rd communication: *Gloor & Zollinger* [1].

reactive) electrophilic reagent was not the cause of the enormous increase in rate under *Olah*'s conditions.

Olah's mechanistic conclusions from the substrate and positional selectivities observed in nitrations with nitronium salts will not be discussed in this paper. Mention will be made however of the rôle of *solvent participation* in the reaction. As postulated by *Olah et al.*, in tetramethylene sulfone a nucleophilic displacement by the basic aromatic substrate on the solvated nitronium ion pairs ($NO_2^{\oplus}X^{\ominus}$) takes place [4].

The low substrate selectivity observed in the nitration of aromatic hydrocarbons with nitronium salts in organic solvents indicates – irrespective of its mechanistic interpretation – that the reactivity of these systems is much higher than that of conventional nitrating media.

By generalising this concept it should therefore be possible to perform substitutions in tetramethylene sulfone with weak electrophiles on aromatic substrates which react very slowly or not at all under conventional conditions with such reagents.

We investigated therefore diazo coupling reactions in tetramethylene sulfone. It is well known that this electrophilic aromatic substitution reaction takes place readily only with aromatic substrates containing a strong *p*-electron donator, *e.g.* with aromatic amines and with phenolate ions. As shown many years ago [5], even phenols, if undissociated, hardly react.

We hoped that, in organic solvents, diazo coupling of compounds like benzene or toluene might be possible. Experiments demonstrated, however, that diazonium salts did *not* react with these substrates in tetramethylene sulfone [6]. Preliminary comparative rate measurements of a diazo coupling reaction with N,N-dimethylaniline showed that the reactivity of the diazonium ion in water and in tetramethylene sulfone was about the same²).

At that time (1965) no explanation for this result was forthcoming. We have now supplemented the kinetic data by additional measurements, and the results will be discussed in the light of the recent results of *Ritchie* and his coworkers. *Ritchie et al.* [8] [9] noted the peculiar reactivity order $N_3^{\ominus} > CH_3O^{\ominus}$ (or $HO^{\ominus}$) $> CN^{\ominus}$ for the rates of reactions of Malachite Green derivatives in various solvents and of substituted benzene diazonium ions in water. The cation-anion combination reactions of these two groups of cations differ drastically from other reactions which have been studied in their sequence of reactivity with nucleophiles. The authors conclude (a) that the anions are reacting directly with a rather non-specifically solvated cation without the necessity of displacing any leaving group, and (b) that the solvent reorganisation energy in the transition state in aprotic solvents is smaller than in hydroxylic solvents.

We measured the rates of the reaction of 4-toluenediazonium salts with N,N-dimethylaniline at 30°C in water, tetramethylene sulfone, acetonitrile and nitromethane in order to

(a) check potential correlations of these cation-molecule reactions with *Ritchie*'s cation-anion combinations,

(b) obtain information on solvent-solute interactions of diazonium ions,

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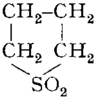
²) These two rate constants were briefly mentioned in a lecture in 1965 [7]; they were recalculated correctly for this paper.

(c) obtain results which would contribute to the mechanistic explanation of our preliminary experiments on solvent effects in diazo coupling reactions as well as to the general understanding of the mechanism of nitrations with nitronium salts in aprotic solvents.

The Table contains our results obtained by the spectrophotometric method under pseudo-first order conditions (excess of N,N-dimethylaniline, see Experimental Part).

Rate constants (k_2) for the reaction between 4-toluenediazonium salts and N,N-dimethylaniline at 30°C[a])

Solvent	Dielectric constant	Dipole moment	E_T-value [11]	Diazonium salt	Yield	k_2 $l \cdot mol^{-1} \cdot s^{-1}$
	44.0	4.8	44.0	$4\text{-}CH_3\text{-}C_6H_4N_2^{\oplus}SO_4H^{\ominus}$	~60%	0.054
CH_3CN	37.5	3.5	46.0	$4\text{-}CH_3\text{-}C_6H_4N_2^{\oplus}SO_4H^{\ominus}$	>90%	0.099
				$4\text{-}CH_3\text{-}C_6H_4N_2^{\oplus}BF_4^{\ominus}$	>90%	0.096
H_2O	78.5	1.8	63.1	$4\text{-}CH_3\text{-}C_6H_4N_2^{\oplus}SO_4H^{\ominus}$	>90%	0.20
CH_3NO_2	38.6	3.1	46.6	$4\text{-}CH_3\text{-}C_6H_4N_2^{\oplus}SO_4H^{\ominus}$	~70%	0.22
				$4\text{-}CH_3\text{-}C_6H_4N_2^{\oplus}BF_4^{\ominus}$	~90%	0.25

[a]) Data in water and tetramethylene sulfone from [7].

Our results demonstrate first of all that the rate of this diazo coupling reaction varies not more than by a factor of 5 in the four solvents. No correlation of the sequence of rates (tetramethylene sulfone $<$ CH_3CH $<$ $H_2O \sim CH_3NO_2$) with conventional solvent parameters (dielectric constant, dipole moment) nor with polarity parameters (Z- or E_T-values) is observable. Hydrogen bonding is not expected to be a decisive factor[3]).

In contrast to this cation-molecule reaction, the cation-anion combination of Malachite Green derivatives with azide ions and cyanide ions is much slower in protic solvents [8]. This is also the case for reactions of molecules with cations other than the diazonium ion, *e.g.* the reaction of trimethylsulfonium nitrate with trimethylamine [10]. In nitromethane this reaction is 119 times faster than in water; its activation energy in nitromethane, ethanol, methanol and water correlates well with *Dimroth*'s E_T- [11] and *Kosower*'s Z-values [12].

Our first conclusion is therefore that the reaction of 4-toluenediazonium salts with N,N-dimethylaniline *does not involve significant solvent reorganisation of the reagents in the formation of the transition state.* In contrast to the cation-anion reactions investigated by *Ritchie et al.* [8] [9], this is the case for *both* reactants. Neither the diazonium ion nor N,N-dimethylaniline are strongly specifically solvated; therefore, desolvation of reactants prior to combination is not a significant contributor to the activation energy.

In addition, no significant influence of the anion in the diazonium salt is observed. This is in contrast to *Olah*'s observations in nitrations with nitronium salts [13] in aprotic media.

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[3]) It may be that the relatively low rate in tetramethylene sulfone is due to the high viscosity of this solvent.

We explain this difference between these two electrophilic aromatic substitutions (as well as the different solvent effect) as follows: A diazonium ion is a very weak electrophile; therefore not only solvation, but also *interactions in ion pairs are weak.* Effects of 'gegenions' and/or solvent molecules are real, but too small to be rationalized. Additional evidence for this characterisation of the diazonium ion comes from our recent result that charge-transfer complex formation of a diazonium ion with 2-naphthol-1-sulfonic acid decreases the rate of diazo coupling only by 26% [14][4]).

The nitronium ion, however, is an extremely reactive electrophile; in protic media its formation might even be rate-limiting [3]. If, in nitration, nitronium salts are used, they are – at least in the solvents used until now – present as solvated ion pairs; the energy of activation for the substitution proper of the aromatic substrates includes always factors which are not due to the formation of the (new) C–N-bond, but to the release of the anion and to desolvation. In contrast to diazo coupling reactions, large variations in rates and in substrate and positional selectivities are to be expected for nitration as a function of the reaction conditions (solvent, 'gegenion', temperature). Rate constants, activation energies etc. are indeed measures of the (bare) electrophilicity of the ion in the case of a diazonium ion; they are, however, composite parameters for a nitrating reagent like the nitronium ion: the 'true' reactivity of the nitronium ion proper is higher than the measured one.

With regard to the electrophile there are (at least) four types of combinations with an aromatic substrate, namely:

(a) bond formation of the electrophile without significant solvent reorganisation and without appreciable energy requirements for ion pair dissociation if the electrophilic reagent is a cation (example: diazo coupling);

(b) concerted nucleophilic displacement of a covalently bonded nucleofugic group of the electrophilic reagent by the aromatic substrate, with or without solvent reorganisation (example: halogenations with molecular halogens);

(c) concerted nucleophilic displacement of associated 'gegenions' and solvent molecules in solvated ion-pair-type electrophiles by the aromatic substrate (example: *Friedel-Crafts* alkylations with *Lewis* acid catalysts, nitration);

(d) concerted nucleophilic displacement of electron acceptors (solvent molecules) in complexes of neutral electrophiles by the aromatic substrate (example: sulfonation with SO_3 [15]).

Superimposed on this classification is, of course, the problem of the structure of the rate-limiting transition state, which covers the wide spectrum from encounter-controlled rates (see for example [16]) through 'early' (π-type-) and 'late' (σ-type-) transition states [17] to those reactions in which the proton release of the aromatic substrate is rate-limiting (see for example [18]).

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[4]) This small decrease is in sharp contrast to *Cerfontain*'s investigations on sulfonation [15], where complex formation with nitro-group-containing solvents (CH_3NO_2) and substrates ($C_6H_5NO_2$) decreased the reactivity of sulfur trioxide by a large amount.

Experimental Part

Preparation and Purification of Materials. – *Nitromethane and Acetonitrile.* Samples of these materials (*Fluka, puriss.* grade) were dried for 3 h at 80 °C with molecular sieves (type 4 A) and fractionally distilled.

Tetramethylene sulfone. Commercial material was distilled at reduced pressure over solid sodium hydroxide. Addition of bromine, followed by two further distillations at reduced pressure over molecular sieves (type 4 A), gave a sample with m.p. 28.0° (reported [16]: 28.5°).

N,N-Dimethylaniline. Commercial material was fractionally distilled twice (b.p. 86°/16 Torr) and stored in the dark. For the kinetic studies samples of this were distilled once more immediately before use.

Other materials were purified by standard methods.

4-Toluenediazonium sulfate. Samples prepared by the method of *Knoevenagel* [19] had a purity of 10–20% as shown by titration with 2-naphthol-3,6-disulfonic acid (R-salt). The following modification of the method gave a product of 97% purity: 4-Toluidine (4.83 g) was dissolved in absolute alcohol (58 g), and sulfuric acid (97%, 5.2 ml) was added slowly with vigorous stirring. Isoamyl nitrite (7.3 ml) was then added to the well-stirred solution over a period of 2.5 h. The temperature of the solution was maintained at 35° throughout the addition and for a further 30 min. The diazonium salt was precipitated with dry ether (100 ml), filtered off, and washed with absolute alcohol (3 × 20 ml) and dry ether (3 × 20 ml). The salt was dried under vacuum over P_2O_5 (15 h, 0,01 Torr) in the dark.

4-Toluenediazonium tetrafluoroborate. This was prepared using the method of *Starkey* [20] and dried over P_2O_5 (15 h, 0.01 Torr) in the dark. Titrations with R-salt showed the diazonium salt to have a purity of 97%.

4-Methyl-4′-(N-N-dimethylamino)-azobenzene. A sample was isolated by filtration from the reaction between 4-toluenediazonium sulfate and N,N-dimethylaniline in water at 40°. It was washed with water (3 × 50 ml), dried and recrystallised from alcohol; m.p. 167°.

Kinetic Methods. – Kinetics were determined by following the increase in optical density of the dye solution with time, using a *Beckman* DB-G spectrophotometer thermostated at 30°. The conditions employed were such that the reactions were pseudo-first order. Pseudo-first order rate constants (k_K) were calculated using the equation:

$$k_K = \frac{1}{t\,(1+q)} \cdot \frac{\ln [\mathrm{D}]_0}{[\mathrm{D}]_0 - [\mathrm{Az}]_t\,(1+q)} ,$$

where

$[\mathrm{D}]_0$ = initial concentration of the diazonium salt,
$[\mathrm{Az}]_t$ = concentration of the dye formed at time t,
$q = ([\mathrm{D}]_0 - [\mathrm{Az}]_\infty)/[\mathrm{Az}]_\infty$.

Values of $[\mathrm{Az}]_\infty$ and $[\mathrm{Az}]_t$ were calculated from graphs of optical density *versus* concentration, which were constructed for the dye in each solvent.

In Nitromethane and Acetonitrile. A solution of N,N-dimethylaniline (1.02×10^{-2}M, 100 ml) was equilibrated at 30° for 30 min. To this was added a solution of the diazonium salt (1.5×10^{-3}M, 2 ml) and the two solutions quickly mixed. A sample was transferred to a 1 cm spectrophotometer cell and the increase in optical density with time was followed at 405 nm and 408 nm, in acetonitrile and nitromethane respectively.

In Water. Solutions of N,N-dimethylaniline (1×10^{-2}M) in water (5 ml) and of the diazonium salt (1×10^{-3}M) in a buffer solution (0.1M NaOAc/0.01M HOAc, 5 ml) were equilibrated at 30° for 10 min. The solutions were quickly mixed. After a certain time the reaction mixture was quenched with R-salt, then 4-methyl-4′-(N-N-dimethylamino)-azobenzene was extracted with chloroform and its concentration determined spectrophotometrically. The experiment was repeated eight times, quenching the reaction at various time intervals.

In Tetramethylenesulfone. The diazonium salt (48.2 mg) was heated in sulfolane (100 ml) at 40° for 80 min. The solution was filtered and the concentration of the diazonium salt was determined by titration of a part of the solution with R-salt. Pseudo-first order rate constants for the formation of the dye formed between the diazonium salt and N,N-dimethylaniline were determined spectrophotometrically using 0.5 cm cells.

BIBLIOGRAPHY

[1] *B. Gloor & H. Zollinger*, Helv. *54*, 563 (1971).

[2] *G. A. Olah, S. J. Kuhn & S. H. Flood*, J. Amer. chem. Soc. *83*, 4571, 4581 (1961), and subsequent papers, summarised by *G. A. Olah & S. J. Kuhn* in 'Friedel-Crafts and Related Reactions' (ed. *G. A. Olah*), vol. III12, p. 1393–1491, Interscience, New York 1965.

[3] *E. D. Hughes, C. K. Ingold*, with *G. A. Benford, E. L. Blackall, R. J. Gillespie, V. Gold, J. Graham, E. R. A. Peeling & G. H. Williams*, J. chem. Soc. *1938*, 929; *1950*, 2441–2552; *1952*, 28.

[4] *G. A. Olah, S. J. Kuhn, S. H. Flood & J. C. Evans*, J. Amer. chem. Soc. *84*, 3687 (1962).

[5] *Z. J. Allan*, Coll. czechoslov. chem. Commun. *16–17*, 620 (1952); *H. Zollinger*, Helv. *36*, 1070 (1953).

[6] *P. Kreienbühl*, Ph. D. thesis ETH Zürich 1966, p. 72–77.

[7] *H. Zollinger*, Chemistry & Ind. *1965*, 885, Table I.

[8] *C. D. Ritchie, G. A. Skinner & V. G. Badding*, J. Amer. chem. Soc. *89*, 2063 (1967).

[9] *C. D. Ritchie & D. J. Wright*, J. Amer. chem. Soc. *93*, two papers in print (1971), presented at the 21st Meeting of the Société de Chimie Physique, Paris, September 22nd to 25th, 1970.

[10] *E. D. Hughes & D. J. Whittingham*, J. chem. Soc. *1960*, 806.

[11] *K. Dimroth, C. Reichardt, T. Siepmann & F. Bohlmann*, Liebigs Ann. Chem. *661*, 1 (1963); *C. Reichardt*, 'Lösungsmittel-Effekte in der organischen Chemie', p. 141–149, 162–164, Verlag Chemie, Weinheim 1969.

[12] *E. M. Kosower*, J. Amer. chem. Soc. *80*, 3253 (1958); *E. M. Kosower*, 'An Introduction to Physical Organic Chemistry', p. 293–338, Wiley, New York 1968.

[13] *G. A. Olah & S. J. Kuhn*, J. Amer. chem. Soc. *84*, 3684 (1962).

[14] *S. Koller & H. Zollinger*, Helv. *53*, 78 (1970).

[15] *J. K. Bosscher & H. Cerfontain*, Rec. Trav. chim. Pays-Bas *87*, 873 (1968); J. chem. Soc. B *1968*, 1524; *H. Cerfontain & A. Koeberg-Telder*, Rec. Trav. chim. Pays-Bas *89*, 569 (1970).

[16] *J. G. Hoggett, R. B. Moodie & K. Schofield*, J. chem. Soc. B *1969*, 1, and literature mentioned therein.

[17] *G. A. Olah, M. Tashiro & S. Kobayashi*, J. Amer. chem. Soc. *92*, 6369 (1970); *G. A. Olah*, Accounts chem. Res. *4*, in print (1971).

[18] *H. Zollinger*, Adv. physic. org. Chemistry *2*, 163 (1964).

[19] *E. Knoevenagel*, Ber. deutsch. chem. Ges. *28*, 2048 (1895).

[20] *E. B. Starkey*, Org. Synth., Coll. Vol. II, 225.

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59. Substituted 9-Oxabicyclo[4.2.1]- and 9-Oxabicyclo[3.3.1]nonanes (Part II[1])

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Summary. The preparation, isolation, structure determination, and some reactions of the two stereoisomers of 2-iodo-9-oxabicyclo[4.2.1]nonane (**9** and **10**) and of 2-iodo-9-oxabicyclo[3.3.1]-nonane (**11** and **12**), respectively, are described.

Iodine cleavage of the [4.2.1]-iodomercuri compound **3** yielded the iodides **9**, **10**, and **11**, and iododemercuration of the [3.3.1]-iodomercuri compound **6** afforded the iodo compounds **9**, **11**, and **12**, respectively. Direct treatment of 4-cycloocten-1-ol (**1**) with iodine in chloroform resulted in the exclusive formation of the two *endo*-iodides **9** and **11**.

Raney nickel treatment as well as lithium aluminium hydride reduction of each individual iodo compound **9**, **10**, **11**, and **12** gave the corresponding unsubstituted 9-oxabicyclononane (**4** or **8**, respectively) with the unaltered skeleton. No rearrangement products could be observed.

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[1] For Part I see [1].