Kinetics. The total addition–alkylation reactions were performed in a vessel constructed to permit separate preheating of the RLi and ArH solutions. The vessel was attached to a vacuum line and was evacuated, flamed, and nitrogen flushed three times prior to charging the reactants. Heating was accomplished within a constant temperature bath capable of maintaining $\pm 0.02°$. Stirring was achieved magnetically. Reaction samples were obtained with a hypodermic syringe inserted through a septum-sealed side arm. Samples were immediately quenched by injection into a large excess of water or methyl iodide. After separation and drying, the organic layer was analyzed by vpc.

Vpc analyses were conducted using an 8 ft × 0.25 in. copper column packed with 20% CDS (cyclohexanedimethanol succinate; Applied Science Laboratories) on Chromosorb P 30–60. Instrumental conditions were: column temperature 208°; helium carrier gas flow rate 80 cc/min, uncorrected. Prior to adoption of kinetic analysis by this method, an intensive vpc investigation was conducted to ensure measurement of all significant aromatic components. Although a dialkylated naphthalene was detected in reactions at 100° and above, the concentration never exceeded *ca.* 2% of the total aromatic content when naphthalene was charged in excess.

For the water-quenched kinetic samples, four peaks were observed (omitting solvent). These components had previously been isolated and identified[2] as: naphthalene, hydrolyzed addition products, 2-*t*-butylnaphthalene, and 1-*t*-butylnaphthalene. For the methyl iodide quenched samples four additional peaks were observed. One peak corresponded in retention time to an authentic sample of 1-methylnaphthalene. The three remaining peaks were assumed to be the possible methylated addition products (the total weight percentage of these three agreed with that predicted by analysis of a duplicate sample quenched with water). No peaks corresponding to 2-methylnaphthalene or to 1- or 2-iodonaphthalene were detected.

For the kinetic analyses by vpc, the weight percentages of the aromatic components were calculated from the measured areas (Disc Integrator) and converted to moles/liter by assuming a constant total aromatic concentration equal to the initial naphthalene concentration. Multiplicative area corrective factors determined from known mixtures were employed to compensate for detector response and thermal conductivity effects.[26]

Reactions from which initial rates were calculated were quenched after times estimated to yield *ca.* 10% reaction. These samples were analyzed by the aforementioned vpc procedure. The initial rate reactions were performed in septum-sealed test tubes, which were evacuated, flamed, and nitrogen flushed three times prior to charging. All transfers of materials were made with Hamilton gas-tight syringes.

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Reactions of Tetranitromethane. I. Kinetics and Mechanism of Nitration of Phenols by Tetranitromethane

Thomas C. Bruice, Maurice J. Gregory,[1] and Sandra L. Walters[2]

Contribution from the Department of Chemistry, University of California at Santa Barbara, Santa Barbara, California 93106.

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Abstract: The reaction of tetranitromethane with phenol, *p*-cresol, *p*-chlorophenol, *p*-cyanophenol, 4-hydroxyacetophenone, and 2,4,6-trimethylphenol (30°, solvent H_2O, $\mu = 0.1$) has been found to follow the rate expression $v = k_r$[phenoxide ion][tetranitromethane] over extended ranges of pH and total phenol concentration ($\rho = -4.25$). All products of the reaction arise from reactions of a single intermediate, the formation of which is rate determining. These products are trinitromethane anion (*ca.* 100% yield), nitrite ion, nitrophenols, and phenol coupling products (*e.g.*, Pummerer's ketone) which can arise only *via* phenoxide free-radical intermediates. For phenol and the *para*-substituted phenols we find nitrophenols to be the minor component of the products with the major portion of the nitro groups appearing as nitrate ion. For the reaction of 2,4,6-trimethylphenol with tetranitromethane, trinitromethane and nitrite ion are quantitatively produced. In 95% ethanol as solvent the reaction has been found to be first order in tetranitromethane and second order in the phenol (determined at one acidity) for 2,4,6-tri-*t*-butylphenol and 2,4,6-trimethylphenol, but first order in tetranitromethane and the phenol when phenol and *p*-cresol are employed. Reaction of 2,4,6-tri-*t*-butylphenol with tetranitromethane produces first the visibly identifiable 2,4,6-tri-*t*-butylphenoxide radical which then yields the coupling product 4-nitro-2,4,6-tri-*t*-butylcyclohexa-2,5-dien-1-one. We propose, as the simplest mechanism to explain these results, initial charge transfer complex formation between tetranitromethane and phenoxide ion (in water a 1:1 complex and in ethanol for cases that are second order in phenol and first order in tetranitromethane a 2:1 complex) followed by the rate-determining step of electron transfer and production of $[\mathrm{XPhO\cdot} + \mathrm{NO_2\cdot} + (\mathrm{NO_2})_3\mathrm{C}^-]$. In steps which are not rate controlling nitrophenol arises from coupling of $\mathrm{NO_2\cdot} + \mathrm{XPhO\cdot}$, phenol condensation products from coupling of $\mathrm{XPhO\cdot}$ species, and nitrite ion by reaction of $\mathrm{NO_2\cdot}$ with additional $\mathrm{XPhO^-}$ and anionic phenol coupling products (see Scheme I).

Tetranitromethane was investigated as a nitrating agent for reactive aromatic compounds by Schmidt and Fischer in 1920.[3] It was reported that high yields of mononitrated aniline derivatives were obtained from reactions with aniline carried out in pyridine–ethanol solution. The reaction of *p*-cresol under similar conditions was reported to provide a 60% yield of 4-methyl-2-nitrophenol. However, attempts to nitrate anethole with the reagent under more drastic conditions led to

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(1) Postdoctoral Fellow, Department of Chemistry, University of California at Santa Barbara, Santa Barbara, Calif.

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formation of 1-phenoxy-1-nitroethane. The reagent appeared to be a rather specific nitrating agent for phenols and aromatic amines though under similar conditions azulene provides, in 81% yield, 1-nitroazulene.[4] The reagent has been recently employed by Vallee and coworkers for the nitration of tyrosyl side chains of proteins and peptides.[5] A reported drawback in the use of the reagent for protein nitration is the fact that it is capable of oxidizing cysteine. Tetranitromethane readily forms charge-transfer complexes with olefins, and this reaction has been used as a means for the detection of unsaturated linkages[3] and the differentiation of double bond types.[6] The mechanism by which tetranitromethane acts as a nitrating agent has not previously been investigated. It has been suggested that the nitration might proceed *via* a nitronium ion[5] or by nitrosation–oxidation.[7]

This paper is concerned with the kinetics and mechanism of reactions of tetranitromethane with phenols in aqueous solution.

Experimental Section

Materials. Tetranitromethane (Aldrich) was used without further purification. Phenol (Baker and Adams reagent grade) and *p*-chlorophenol (Eastman Red Label) were redistilled, bp 178–180 and 85° (5 mm), respectively. *p*-Cyanophenol, 2,4,6-trimethylphenol (Aldrich), and 4-hydroxyacetophenone (Eastman, practical) were recrystallized from mixtures of carbon tetrachloride and chloroform, mp 112–113, 68–69, and 108–109°, respectively, and *p*-cresol (Matheson, redistilled) was recrystallized from petroleum ether (bp 30–60°), mp 34–35°. 2,4,6-Tri-*t*-butylphenol (Aldrich) was crystallized from *n*-hexane, mp 129–131°. Tris(hydroxymethyl)-aminomethane (Matheson Coleman and Bell), glycine (Fisher reagent), sulfanilic acid (Mallinckrodt Analytical Reagent), and β-naphthylamine (Aldrich) were employed without further purification. Trifluoroethanol (Matheson Coleman and Bell) was redistilled, bp 75–76°. Nitrophenols were prepared according to literature procedures: 4-cyano-2-nitrophenol, mp 146–147°,[8] 4-chloro-2-nitrophenol, mp 87–88°.[9] 4-Methyl-2-nitrophenol (Aldrich) was recrystallized from petroleum ether (bp 30–60°), mp 33–34°. 2-Nitro- and 4-nitrophenols (Eastman White Label) were crystallized from carbon tetrachloride, mp 43–44 and 112–113°, respectively. Trinitromethane (K & K Laboratories) was used without further purification.

Reaction of *p*-Cresol with Tetranitromethane under Preparative Conditions. Tetranitromethane (3.5 ml; 0.03 mol) was added to a stirred solution of 6.6 g (0.06 mol) of *p*-cresol dissolved in 300 ml of 0.11 *N* KOH at 0° over a period of 90 min. After stirring the solution for an additional hour, it was extracted with ether (five 50-ml portions); the ether layers were collected, and the aqueous phase was adjusted to pH 4 with HCl and extracted with chloroform (five 50-ml portions). A portion of the remaining aqueous phase (0.1 ml) was tested for nitrite according to the procedure of Kolthoff and Elving.[10] A strongly positive reaction was obtained.

Neutral Products. The ether solution was dried ($MgSO_4$) and the ether distilled off. The brown oil obtained (2.02 g) showed strong bands in its infrared spectrum (CH_2Cl_2) at 1680, 1510, and 1010 cm^{-1}. The oil was extracted with refluxing *n*-hexane (two 50-ml portions). Evaporation of the hexane left a yellow low-melting solid (990 mg). Recrystallization of this solid from *n*-hexane gave an off-white solid (450 mg), mp 123–124°, undepressed on mixing with a specimen of 1,2,10,11-tetrahydro-6,11-dimethyl-2-oxodibenzfuran (I).[11] An oxime was prepared according to Westerfield and Lowe,[12] mp 189–192°, elevated to 196–198° on mixing with an authentic specimen of the oxime of 1,2,10,11-tetrahydro-6,11-dimethyl-2-oxodibenzfuran.

The residue from the hexane extractions was dissolved in ether and on addition of hexane yielded a pale yellow precipitate, mp 72–110°. Attempts to purify this material further by recrystallization or precipitation were unsuccessful, and the best melting point obtained was 78–115°.

Acidic Products. The chloroform extracts were dried ($MgSO_4$) and evaporated, leaving a brown tar (3.9 g) which was steam distilled. The distillate (350 ml) was extracted with chloroform (four 50-ml portions), and the residue was extracted with chloroform (five 50-ml portions).

Steam-Volatile Products. The chloroform extracts were dried ($MgSO_4$) and the solvent was removed to leave a yellow low-melting solid (1.09 g). Recrystallization of the solid from *n*-hexane gave 4-methyl-2-nitrophenol (0.81 g), mp 33–34°.

Steam-Involatile Products. Distillation of solvent from the chloroform extracts left a tar from which no identifiable material could be isolated by extraction with *n*-hexane and then benzene. Neither the extracts nor the residue was appreciably soluble in 1 *N* KOH.

Reaction of 2,4,6-Tri-*t*-butylphenol with Tetranitromethane. Tetranitromethane (0.76 g; 0.004 mol) was added slowly to a stirred solution of 2,4,6-tri-*t*-butylphenol (1.0 g; 0.0038 mol) and KOH (0.25 g; 0.0047 mol) in ethanol (20 ml). After the bright green solution became yellow (~1 hr) the solid (1.25 g) which had precipitated was filtered off. The solid was recrystallized from ethanol to give 4-nitro-2,4,6-tri-*t*-butylcyclohexa-2,5-dien-1-one (II) (0.34 g, 30%), mp 81–82°, undepressed on mixing with an authentic specimen prepared by the action of nitric acid on 2,4,6-*t*-butylphenol.[13]

The infrared spectrum (KBr) of the two samples were identical (major bands at 3000, 1670, 1650, 1550, 1350, and 1330 cm^{-1}). A yellow residue from the recrystallization was identified as the potassium salt of nitroform (0.48 g, 50%) by its ultraviolet spectrum (λ_{max} 350 mμ).

Further II was obtained on concentrating the mother liquors (0.18 g, 15%), mp 78–81°.

Kinetic Studies. Apparatus. Absorbance measurements were made on a Zeiss PMQ II spectrophotometer equipped with a Zieler automatic cell positioner, or a Gilford Model 220 recording spectrophotometer. Kinetic solutions were maintained at 30 ± 0.1° by circulating water at this temperature through the cuvette holder (Zeiss) or through Beckman double thermospacers (Gilford). Reaction rates too fast to follow visually were followed on a Durrum-Gibson 13001 stopped-flow apparatus, with Kel-F cells. pH measurements were made with a Radiometer Model 22 pH meter with a PHA 630 scale expander using a combined glass-calomel electrode (Radiometer G.K. 2021C). The electrode was thermostated at the temperature of the kinetic runs.

Kinetics. The rate of disappearance of tetranitromethane in various buffers was followed by measuring the increase in absorbance at 350 mμ. A stock solution of tetranitromethane in methanol (1×10^{-2} *M*) was prepared. One drop of this solution was added to the cuvette in which the reactions were carried out. Reactions were followed to three to four half-lives. Pseudo-first-order rates were obtained from the slopes of plots of $-\log [(OD_\infty - OD_t)/(OD_\infty - OD_0)]$. The pH of the solutions was measured before and after the reaction. Serial dilutions were carried out (unless otherwise stated) with 0.1 *M* KCl solution when the phenols themselves were the buffers, and with the auxiliary buffer when these were used.

Kinetic solutions in ethanol were prepared by addition of KOH to solutions of the phenols in 95% ethanol, using $(CH_3)_4NCl$ to maintain ionic strength at 0.1. Serial dilutions were carried out with 0.1 *M* $(CH_3)_4NCl$ in 95% ethanol.

Product Analyses. These were carried out on duplicates of kinetic solutions. Analyses for nitrophenols and trinitromethane were carried out spectrophotometrically by solving the simultaneous equation for the absorbances at 350 mμ and the λ_{max} (Table I) of the phenol. The absorbance of a mixture of components at a

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Table I. Spectroscopic Data for Nitration Products

Anion	λ_{max}, mμ	ϵ_{max}
Trinitromethane	350	14,000
o-Nitrophenol	415	4,750
p-Nitrophenol	400	14,000
2-Methyl-2-nitrophenol	435	4,400
4-Chloro-2-nitrophenol	430	4,500
4-Cyano-2-nitrophenol	400	4,250

Table II

	At t_∞		
Phenol	$C(NO_2)_3^-$, %	Nitrophenol, %	NO_2^-, %
p-Cresol	101 ± 2	28.6 ± 2.8	64.8 ± 0.5
p-Chlorophenol	99.8 ± 0.25	25.6 ± 0.25	70.8 ± 0.25

Table III. Rate Constants for the Reaction of Tetranitromethane with Five Phenols and Hydroxide Ion at 30° in Water with $\mu = 0.1$

4-Substituent of phenol	k_2, M^{-1} min^{-1}	k_r, M^{-1} min^{-1}	k_n, M^{-1} min^{-1}	pH range	No. of k_{obsd}	No. of pH's
CH_3	5.1×10^4	3.30×10^4	1.4×10^4	6.95–8.9	30	6
H	2.0×10^3	1.56×10^3	$1.6 \times 10^{2\,a}$ $2.6 \times 10^{2\,b}$		30	5
Cl	5.7×10^2	3.20×10^2	1.7×10^2	8.38–9.68	30	6
CH_3CO	1.1			7.06–8.45	30	5
NC	0.26	0.22	0.050	7.23–8.60	29	5
2,4,6-$(CH_3)_3$	1.1×10^7	1.0×10^7		6.12–7.04	25	5

[a] *ortho.* [b] *para.*

given wavelength is the sum of the absorbances of the two components (absorbance, $A = C_X\epsilon_X + C_Y\epsilon_Y$). By measuring the absorbance at two wavelengths (1, 2), the concentration of a component X (C_X) can be found from the solution of the equations giving the total absorbances

$$C_X = (A_1\epsilon_{Y_2} - A_2\epsilon_{Y_1})/(\epsilon_{X_1}\epsilon_{Y_2} - \epsilon_{X_2}\epsilon_{Y_1}) \qquad (1)$$

where A_1, A_2 are the absorbances at wavelengths 1 and 2, ϵ_{X1}, ϵ_{X2}, ϵ_{Y1}, ϵ_{Y2} are the molar extinction coefficients at the two wavelengths. Solutions were analyzed for nitrite ion by the method of Kolthoff and Elving.[10]

No variation in the amount of nitrite ion determined was found when *p*-cresol was extracted from the kinetic solutions with carbon tetrachloride before analysis, showing that the phenol did not interfere with the nitrite determinations.

For phenol, the *o*- and *p*-nitrophenols were separated by extraction with carbon tetrachloride. Kinetic solutions (10 ml) were adjusted to pH 2–4 and extracted with carbon tetrachloride (three 3-ml portions). The aqueous solution was centrifuged and 1 *M* KOH (5 ml) was added. This solution was analyzed for trinitromethane and *p*-nitrophenol as before. The carbon tetrachloride extract was washed with water (two 3-ml portions) and with 1 *M* KOH (two 2.5-ml portions). The alkaline solutions were diluted to 10 ml, and the absorption at 420 mμ was used to estimate the yield of *o*-nitrophenol.

Stoichiometry of Reaction of Tetranitromethane with Phenols. The per cent yields of nitroform, nitrite ion, and nitrophenol were determined at completion of the reaction of solutions 1.0×10^{-3} *M* in the phenol and tetranitromethane (30°; solvent H_2O, $\mu = 0.1$ by borate buffer; pH 8.9). The analytical procedures were those previously described. The averaged results of two experiments each for *p*-cresol and *p*-chlorophenol are presented in Table II. In the absence of a phenol, the buffered solution at t_0 was found to contain 2.5 ± 1.5% trinitromethane and 8 ± 1% nitrite ion. On standing a period of time equal to t_∞ for the reaction of tetranitromethane with *p*-cresol, the same buffer blank contained 3.57% trinitromethane and 4.45% nitrite ion and on standing a period of time equal to t_∞ for reaction of tetranitromethane with *p*-chlorophenol, the buffer blank contained 22.3% trinitromethane and 23.5% nitrite ion. For *p*-chlorophenol, after correction for the blank reaction ~60% of the nitrite ion arose from reaction of tetranitromethane with the phenol and ~80% of the trinitromethane arose from the same reaction. If ~30% nitrated phenol is produced in a 1:1 reaction of tetranitromethane and *p*-chlorophenol then 50% of the trinitromethane arose from the same reaction that produced 60% nitrite ion. Therefore, from the nitrite-producing reaction the ratio of nitroform to nitrite ion is 1:1.2. For *p*-chlorophenol the same reasoning leads to a ratio of trinitromethane to nitrite of 1:0.85. These results in borate buffer at pH 8.9 suggest that in the nitrite-producing reaction the disappearance of 1 mol of phenol leads to the production of 1 mol of nitroform and 1 mol of nitrite ion (±20%).

Results

The second-order rate constants for the reaction of tetranitromethane (4NM) with phenols (H_2O; 30°; $\mu = 0.1$) are provided in Table III. The rate of trinitromethane anion (3NM) formation was followed spectrophotometrically [employing tris(hydroxymethyl)-aminomethane or glycine buffers when necessary] under the pseudo-first-order conditions of total phenol concentration ([phenol$_T$]) ≫ [4NM]. The concentration of phenol$_T$ ranged from 0.01 to 0.1 *M* (with *p*-cresol half these values) at each of five or six constant pH values and kinetic studies were carried out at five different concentrations at each pH. Plots of the pseudo-first-order rate constants (k_{obsd}) *vs.* [phenol$_T$] at constant pH were linear of slope k_2' and intercept zero (Figure 1).

$$k_{obsd} = k_2'[\text{phenol}_T] \qquad (2)$$

Plots of k_2' *vs.* $K_a'/(K_a' + a_H)$ (or for phenol and *p*-cresol where experimental conditions were such that $a_H \gg K_a'$ *vs.* K_a'/a_H) were found to be linear of slope k_2 and intercept zero (Figure 2).

$$k_2' = \frac{k_2K_a'}{K_a' + a_H} \qquad (3)$$

From (2) and (3)

$$k_{obsd} = \frac{k_2K_a'}{K_a' + a_H}[\text{phenol}_T] \qquad (4)$$

and

$$\frac{-d[4NM]}{dt} = k_2[4NM][XPhO^-] \qquad (5)$$

The over-all second-order rate constant for reaction of 4NM with phenoxide ion (k_2) was found to be invariant on change of concentration of buffers. No contribution of a hydroxide-catalyzed hydrolysis of 4NM could be detected as shown by the zero intercept of the plots of k_{obsd} *vs.* [phenol$_T$] at constant pH. *Since the reaction of 4NM with phenols is not dependent on a_H or buffer but only on the concentration of phenoxide ions, one must conclude that all products* (*i.e.*, 3NM, NO_2^-, and nitro-

Table IV. Product Analyses for the Reaction of Four Phenols with Tetranitromethane at 30° in H_2O (μ = 0.1)[a]

4-Substituent of phenol	pH	Total concn of phenol[b,c] 0.1 *M*			Total concn of phenol[b,c] 0.05 *M*			Total concn of phenol[b,c] 0.01 *M*			Mean NO_2^- yield, %	Mean nitrophenol yield, %	Total, %
		3NM, %	NO_2^-, %	NP, %	3NM, %	NO_2^-, %	NP, %	3NM, %	NO_2^-, %	NP, %			
CH_3	10.6	104	66	29	103	66	27	103	67	26	65	28	93
	10.1	102	55	30	102	65	28	101	66	31			
	9.3	101	62	31	97	64	26	98	56	26			
	8.8	102	63	30	92	66	29	104	67	28			
	7.0	99	67	30	102	67	29	102	67	26			
H	10.7	92	73	8/15	90	75	8/13	90	78	8/11	77	8 (*o*)	98
	10.0	90	75	8/16	96	78	8/16	86	82	8/13		13 (*p*)	
	9.4	73	75	8/9	92	78	8/10	90	77	8/10			
Cl	9.7	105	59	25	103	52	28	103	51	27	57	29	86
	8.3	99	60	32	106	50	28	101	60	30			
CN	8.5	97	87	20	98	81	20	93	82	18	84	19	103
	7.1	97	89	19	105	77	19	71	87	27			

[a] Abbreviations used: 3NM = trinitromethane, NP = nitrophenol. [b] Yields of NO_2^- and NP have been corrected for 100% yield of trinitromethane. [c] For phenol the yields of *o*- and *p*-nitrophenols are shown as *ortho*/*para*.

phenols) *are formed in a reaction whose rate-determining step is first order in 4NM and first order in phenoxide ion.*

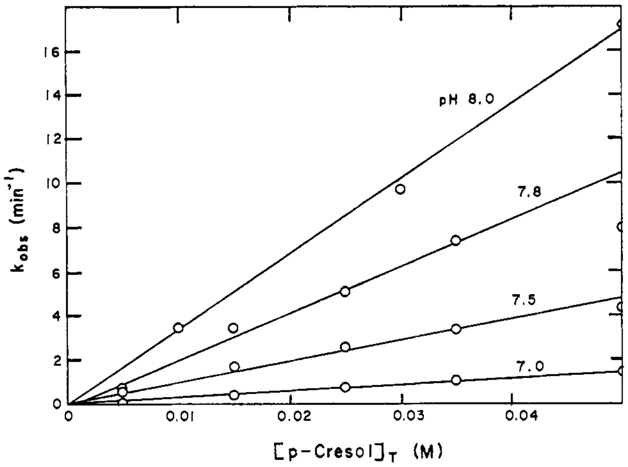


Figure 1. Dependence of the pseudo-first-order rate constants for the reaction of tetranitromethane with *p*-cresol on the concentration of *p*-cresol at four pH's.

From the mean yields of nitrophenols and nitrite ion given in Table IV (see Experimental Section), the overall rate constants for the formation of nitrophenols (k_n) and nitrite ion (k_r) were calculated (Table III). The rate constants were obtained by multiplying the rate constant for the disappearance of tetranitromethane (k_2) by the mean fractional yield of the product, *i.e.*

$$k_n = \frac{k_2 \times \%\,\mathrm{NP}}{100}$$
$$k_r = \frac{k_2 \times \%\,\mathrm{NO_2^-}}{100} \qquad (6)$$

Inspection of Table IV reveals that for phenol and the various *para*-substituted phenols the yield of trinitromethane is quantitative but the yield of nitrophenols amounts to but *ca.* 20–30% while nitrite ion production accounts for *ca.* 55–80%. For 2,4,6-trimethylphenol no nitrated products could be detected, whereas 3NM and nitrite production were quantitative.

For *p*-cresol and *p*-cyanophenol no variation in the yield of the corresponding nitrophenol could be detected when the ionic strength was varied from 0.01 to 1.0 *M*, using potassium chloride. However, increasing ionic strength (11 k_{obsd} values at pH 9.4 between μ = 0.05 and 1.0) favored the formation of 2-nitro-4-chlorophenol according to eq 7.

$$\%\ \text{nitrophenol} = 27.5 + 13\mu \qquad (7)$$

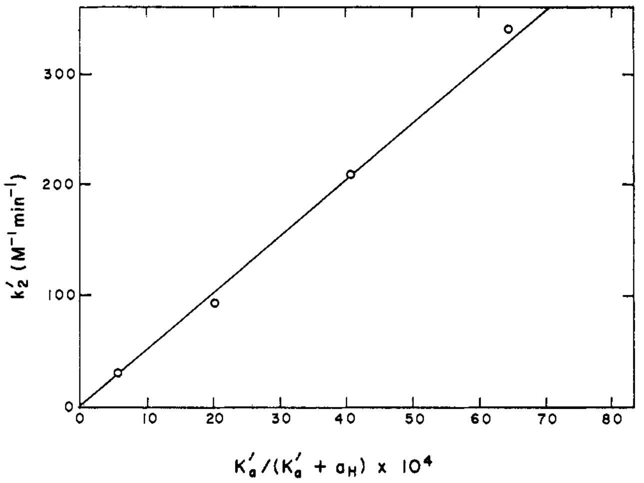
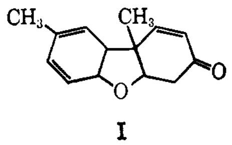


Figure 2. Dependence of the pH-dependent second-order rate constants (k_2') for the reaction of *p*-cresol with tetranitromethane on the mole fraction of *p*-cresolate anion present ($K_a'/(K_a' + a_H)$).

For *p*-cresol it was possible to establish on a preparative scale that in addition to the expected products, nitrated *p*-cresol (~23% yield) and nitrite ion, there was also produced, in 30% yield, 1,2,10,11-tetrahydro-6,11-dimethyl-2-oxodibenzfuran (Pummerer's ketone; I) plus unidentifiable and apparently polymeric products. Though *p*-cresol was employed in a twofold excess over 4NM no *p*-cresol could be recovered. Since Pum-



I

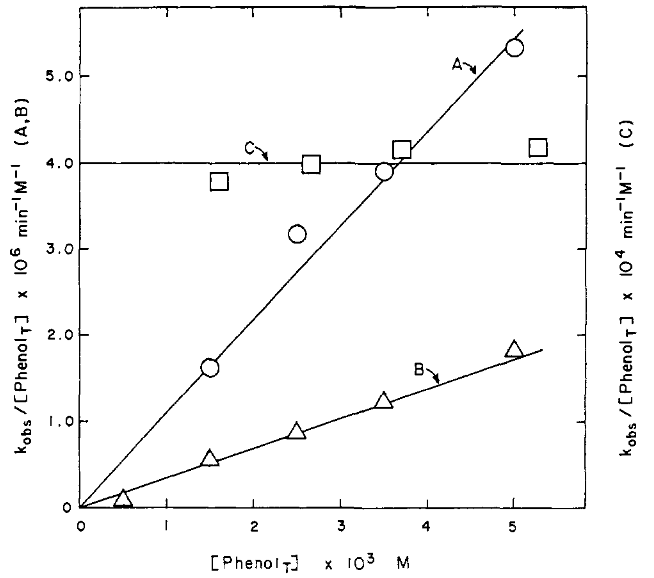
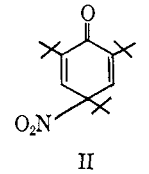


Figure 3. Variation in the function k_{obsd}/[phenol$_T$] with [phenol$_T$] for the reaction of three phenols with tetranitromethane in 95% ethanol (A = 2,4,6-trimethylphenol, B = 2,4,6-tri-*t*-butylphenol, C = *p*-cresol).

merer's ketone is obtained only *via* free-radical oxidation of *p*-cresol[11,14] (in addition to unidentified tars such as thoseo btained in our case), this experiment establishes the generation of phenoxide radicals. Experiments with *p*-cresol and *p*-chlorophenol establish that 1 mol of the phenol is all that is required for disappearance of 1 mol of 4NM and that the 4NM can be quantitatively accounted for as 3NM, nitrite ion, and nitrophenols (see Experimental Section). The consumption of 2 mol of *p*-cresol in the presence of 1 mol of 4NM is then to be attributed to the formation of polyphenols.

Tri-*t*-butylphenol is known to yield a relatively stable free radical.[15] The reaction of this phenol with 4NM in H_2O could not be investigated due to the insolubility of the phenol in this solvent. The reaction was, therefore, investigated in ethanol. When 4NM was added to an ethanolic solution of tri-*t*-butylphenol, there appeared immediately the characteristic blue color of the phenoxide radical. With time the color faded, and from the precipitate could be isolated, in 45% of theory, 4-nitro-2,4,6-tri-*t*-butylcyclohexa-2,5-dien-1-one (II).



II

Compound II could reasonably be produced *via* the coupling of tri-*t*-butylphenol and nitrite free radicals.

The kinetic rate expression for formation of 3NM from 4NM as a function of [tri-*t*-butylphenol$_T$] in 95% ethanol at 50% neutralization of phenol with KOH was found to be first order in 4NM and second order in [tri-*t*-butylphenol$_T$]; see Figure 3. The value of k_3 in the expression k_3[4NM][phenoxide]^2 was found to be k_2 = 3.6 × 10^8 l.^{2} mol^{-2} min^{-1}. To ascertain if the change of order from first to second in [phenol$_T$] was due to the nature of the phenol or to a general change of the kinetics of the reaction of 4NM with phenols on going from water to ethanol, we also investigated the reactions of 4NM with 2,4,6-trimethylphenol, phenol, and *p*-cresol in ethanolic solution. The data for three of these phenols are contained in Figure 3 from which it can be seen that the reaction of 2,4,6-trimethylphenol is second order in [phenol$_T$] while the reaction of phenol and *p*-cresol remains first order in [phenol$_T$]. At 25% neutralization the calculated rate constant (k_3) is 1.05 × 10^9 l.^{2} mol^{-2} min^{-1} for 2,4,6-trimethylphenol and at 50% neutralization the value of k_2 is 3.9 × 10^4 and 3.85 × 10^3 l. mol^{-1} min^{-1} for *p*-cresol and phenol, respectively. Thus, the order changes from first to second in [phenol$_T$] for 2,4,6-trimethylphenol but remains first order for *p*-cresol and phenol when the solvent is changed from water to 95% ethanol.

In the absence of phenol, 4NM slowly yields 3NM in aqueous solution. Addition of trifluoroethanol (up to 0.5 *M*) to a carbonate buffer solution at pH 9.86 was found not to affect the rate of 4NM disappearance.

Discussion

The reaction of tetranitromethane (4NM) in water with all phenols investigated obeys rate expression 5. The second-order rate constants for these reactions are given in Table III. The reactions of *p*-cresol and phenol have been investigated at pH values down to 3 pH units below their pK_a's in order to ascertain whether there was any significant contribution from terms involving the neutral phenols. Such terms could not be detected (see Figure 2), so that the second-order rate constants for reaction of 4NM with XPhOH must be at least 10^4 times smaller than for the reaction of 4NM with XPhO$^-$ The pseudo-first-order rate constants for the reactions of *p*-cresol and phenol were found to be independent of the concentrations of tris(hydroxymethyl)aminomethane or glycine used to maintain constant pH during the reaction. The reaction would therefore appear to be insensitive to nucleophilic, general acid, or general base catalysis. For the other phenols no terms involving hydroxide and phenolate ion and tetranitromethane concentrations could be detected so the reaction is not subject to specific base catalysis unless it involves a term such as (8), which is kinetically indistinguishable from eq 5. The best correlation of the rate constants with a

$$\frac{-d[C(NO_2)_4]}{dt} = k_3[OH^-][PhOH][C(NO_2)_4] \qquad (8)$$

Hammett-type linear free energy relationship was to σ^- (Figures 4, 5, and 6). The $\rho\sigma^-$ plot (Figure 4) has a slope of −4.25.

Four types of mechanism for the nitration of phenols by tetranitromethane have been considered. These are nitration *via* nitronium ion, nitro radical, O-nitration of the phenol, and direct reaction between the phenol and tetranitromethane.

It seemed possible that O-nitration of the phenol might be involved (eq 9). An intramolecular rearrangement of the phenyl nitrate, analogous to the rearrange-

$$PhO^- + C(NO_2)_4 \longrightarrow C^-(NO_2)_3 + PhONO_2 \longrightarrow NO_2PhOH \qquad (9)$$

ment of nitramines,[16] would lead to a nitrophenol. It

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(14) A. I. Scott, *Quart. Rev.* (London), 14, 1 (1965).

(15) H. Mauser and B. Nickel, *Angew. Chem.*, 77, 378 (1965).

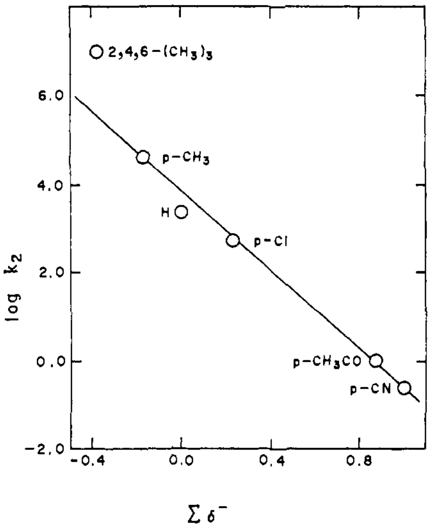


Figure 4. Dependence of the second-order rate constants (k_2) for the reaction of six phenols with tetranitromethane on σ^-.

would be expected that this rearrangement woud lead predominantly to an *o*-nitrophenol. The nitration of phenol with tetranitromethane led to an *ortho*:*para* ratio of 1 : 1.5, which is not consistent with this rearrangement. Furthermore, trifluoroethoxide ($pK_a' = 12.8$) does not act as a nucleophile toward tetranitromethane, and it seems unlikely, therefore, that phenol ($pK_a' = 10$) would. Therefore, this possible mechanism may be discarded. The nitration of phenols with concentrated nitric acid proceeds *via* electrophilic substitution by nitronium ion.[17] It has been suggested[5] that tetranitromethane is capable of ionization to nitronium ion and trinitromethane anion, and that nitronium ion is the species involved in the nitration of phenols by this reagent (10). There is no significant contribution of a

$$(NO_2)_3CNO_2 \underset{k_1}{\overset{k_2}{\rightleftharpoons}} (NO_2)_3C^- + N^+O_2 \xrightarrow[k_3]{PhO^-} O_2NPhOH \qquad (10)$$

reaction involving this ionization in the hydrolysis of tetranitromethane since the reaction is first order in both 4NM and hydroxide ion and no autoinhibition of the reaction by trinitromethane anion could be detected. Also, from a comparison of the pK_a's of trinitromethane and the phenols (<1 and 7–10) and the large excess of phenoxide ion over trinitromethane anion it would not be anticipated that reaction of nitronium ion with trinitromethane anion would be comparable in rate to the reaction with phenoxide. Thus, it would be likely that if (10) prevailed the reaction would be first order in tetranitromethane and zero order in phenoxide ion. This is clearly not the case (see Figure 2). If the ionization of tetranitromethane should occur within a caged charge transfer complex of tetranitromethane and phenoxide ion ($3NM^- + NO_2^+ + PhO^-$) then the kinetics would be as observed experimentally. Such a process cannot be discarded on a kinetic basis. However, this process could not account for the production of nitrite ion accompanied by a 100% yield of $3NM^-$.

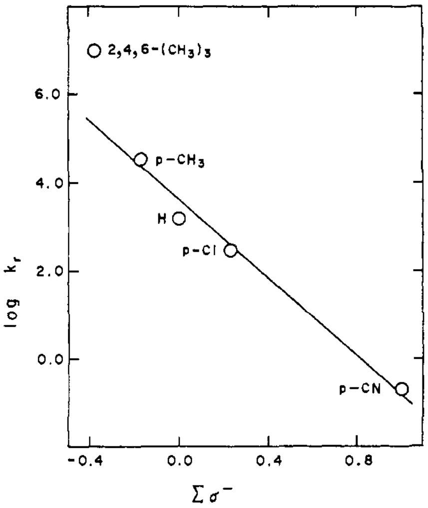


Figure 5. Dependence of the second-order rate constants for formation of nitrite ion (k_r) from the reaction of five phenols with tetranitromethane on σ^-.

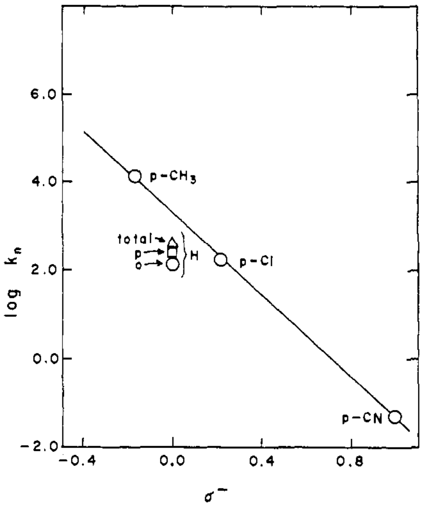
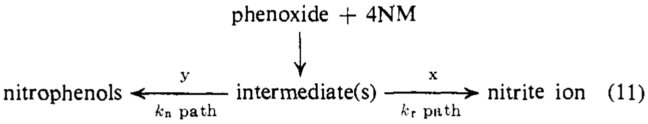


Figure 6. Dependence of the second-order rate constants (k_n) for nitration of four phenols with tetranitromethane on σ^-.

It can be seen (Table IV) that for the reaction of all phenolate ions with 4NM, the yield of trinitromethane is essentially quantitative. However, the yields of nitrophenols are in the range of 20–30%, and for a given phenol the yield is independent of pH and concentration of the phenol. Similarly the yield of nitrite, which accounts for most of the remaining nitro groups, is also independent of pH and concentration of the phenol. From the yields of nitrophenols and nitrite ion the rate constants for the formation of these products from tetranitromethane have been calculated (Table III). The lack of sensitivity of the product ratios to pH, phenol concentration, or the nature of the *para*-substituent groups establishes that nitrophenols and nitrite ion arise from a common steady-state intermediate (*e.g.*, eq 11).



$$\begin{tikzcd} & \text{phenoxide} + \text{4NM} \arrow[d] & \\ \text{nitrophenols} & \text{intermediate(s)} \arrow[l, "y", "k_n\ \text{path}"'] \arrow[r, "x", "k_r\ \text{path}"'] & \text{nitrite ion} \end{tikzcd} \qquad (11)$$

It is unlikely that nitrite ion could be obtained in an ionic reaction. Schmidt[18] reported that tetranitromethane undergoes hydrolysis in strong alkali to give

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(16) E. D. Hughes and G. T. Jones, *J. Chem. Soc.*, 2678 (1950).

(17) C. A. Bunton, E. D. Hughes, C. K. Ingold, D. F. H. Jacobs, M. H. Jones, G. J. Minkoff, and R. I. Reed, *ibid.*, 2628 (1950).

(18) E. Schmidt, *Chem. Ber.*, 52, 400 (1919).

nitrite ion and carbonate ion. However, the stoichiometry of this reaction (12) would require that 4 moles

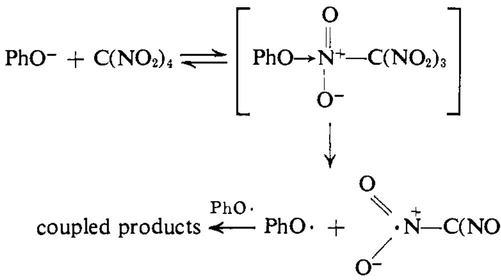
$$C(NO_2)_4 + 6OH^- \longrightarrow CO_3^{2-} + 4NO_2^- + 3H_2O \qquad (12)$$

of nitrite be obtained per mol of tetranitromethane. In the nitration experiments reported here, the simultaneous formation of 70–80% nitrite ion would require a maximum yield of trinitromethane of 80–83% if (12) were responsible for the nitrite production. In fact, the yields of trinitromethane were close to 100% in all cases. Thus, the reaction reported by Schmidt[18] could not account for the amount of nitrite ion produced, and this product must arise in some other manner. The isolation of a phenoxy radical coupling product (Pummerer's ketone I) from the nitration of *p*-cresol suggests that nitrite ion might arise from the reaction in which free radicals are produced. The simplest mechanism would involve homolysis of tetranitromethane and subsequent electron transfer from phenolate ion (13). This mechanism is of course not in accord with

$$\begin{array}{ccccc} C(NO_2)_4 & \rightleftharpoons & \dot{C}(NO_2)_3 & + & \dot{N}O_2 \\ & & \downarrow{\scriptstyle PhO^-} & & \downarrow{\scriptstyle PhO^-} \\ & & C^-(NO_2)_3 + PhO\cdot & & NO_2^- + PhO\cdot \end{array} \qquad (13)$$

the fact that the reaction is first order in phenoxide unless the rate of recombination of the primary radicals is much faster than the rate of reaction of these radicals with phenoxide ion. It seems more likely that reaction of nitro radical with phenoxide ion would be faster than its reaction with the stabilized trinitromethyl radical.

The radical-forming reaction must, therefore, involve an intermediate. It is known that tetranitromethane will form charge-transfer complexes with olefins in chloroform, and that irradiation of these complexes produces free radicals,[19] with an electron being donated to the tetranitromethane. Such reactions were not noted with benzene. A similar reaction under our conditions with the readily oxidized phenols would seem quite possible, and can be formulated as in (14).



(14)

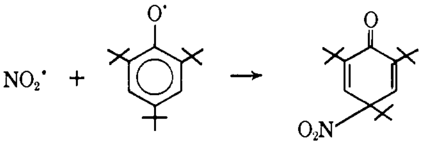
III

Here electron transfer is pictured as being complete, although the possibility of a radical pair as an intermediate cannot be discounted. The fate of the radical ion III is most likely that of heterolysis to nitro radical and trinitromethane anion as shown by the experiments with tri-*t*-butylphenol. Attempts to identify the radicals from the reaction of tetranitromethane by epr methods were unsuccessful, as no spectrum was obtained.

The nitro radical is thought to be involved in the nitration of olefins by dinitrogen tetroxide,[20] although nitration of phenols by this species has not been confirmed. The reaction of *m*-nitrophenol with tetranitromethane yields 86% nitrite ion, showing the nitration has been suppressed by the *m*-nitro group. *A priori* it might have been expected that nitration by a radical process would be enhanced by stabilization of the initial radical by the nitro group, whereas nitration processes in which an incipient positive charge is generated at the 3 position would be suppressed. However, it should be noted that the nitro radical has a degree of electrophilic character, and might also react much more slowly with *m*-nitrophenol, so this experiment is not conclusive. With 2,4,6-trimethylphenol in water, no aromatic nitration products could be detected and a 100% yield of $3NM^-$ and nitrite ion was obtained. If 4NM undergoes scission in a charge-transfer complex to yield $NO_2\cdot$ and NO_2^+ then one must make the additional posulation that the NO_2^+ is recaptured by $3NM^-$ much faster than by water (15). If this were not so, a

$$\text{C.T.C}\begin{array}{l} \nearrow\, 3NM^- + NO_2^+ + PhO^- \\ \searrow\, 3NM^- + NO_2^{\cdot} + PhO^{\cdot} \end{array} \qquad (15)$$

100% yield of NO_2^- could not be obtained. If in place of 2,4,6-trimethylphenol the reaction is studied with 2,4,6-tri-*t*-butylphenoxide in ethanol a 45% yield of the ring-nitrated product II is obtained. The color of the reaction mixture clearly established the immediate formation of 2,4,6-tri-*t*-butylphenol free radicals. These results suggest (16). Free-radical coupling products of



(16)

the general type represented by (16) have been reported.[21] In water the reaction of 4NM with 2,4,6-trimethylphenoxide is first order with respect to both species whereas in ethanol it is first order in 4NM and second order in phenoxide. The same result was obtained with the tri-*t*-butylphenol in ethanol. This suggests complexes in H_2O of a 1:1 nature and in ethanol of a 1:2 nature.

The simplest mechanism which is in accord with the established facts is presented in Scheme I. In Scheme I, reversible formation of a charge-transfer complex

Scheme I

Rate-determining steps

$$XPhO^- + 4NM \overset{K_\pi}{\rightleftharpoons} \text{charge-transfer complex}$$

$$\text{charge-transfer complex} \xrightarrow[k_e]{e^-\ \text{transfer}} [XPhO\cdot + NO_2\cdot + (NO_2)_3C^-]$$

Fast steps

$$[XPhO\cdot + NO_2\cdot + (NO_2)_3C^-] \xrightarrow{k_a} NO_2XPhO^- + (NO_2)_3C^-$$

$$[XPhO\cdot + NO_2\cdot + (NO_2)_3C^-] \longrightarrow XPhO\cdot + NO_2\cdot + (NO_2)_3C^-$$

$$NO_2\cdot + XPhO^- \xrightarrow{k_e} XPhO\cdot + NO_2^-$$

$$n\,XPhO\cdot \longrightarrow \text{coupling products}$$

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(19) C. Lagercrantz and M. Yhland, *Acta Chem. Scand.*, **16**, 1807 (1962).

(20) T. E. Stevens and W. D. Emmons, *J. Amer. Chem. Soc.*, **80**, 338 (1958).

(21) As an example see: D. A. Bolon, *J. Org. Chem.*, 32, 1584 (1967).

is followed by electron transfer from the phenoxide moiety to 4NM and scission of the N–C bond of 4NM in the rate-determining step. Tetranitromethane is known to readily form charge-transfer complexes,[6] and bond rupture following electron transfer is an established process.[22] The products of the reaction then arise in steps that are kinetically competitive and faster than C–N bond scission. Assuming a steady state in the caged product of the k_e step, the rate of $3NM^-$ production is given by

$$v = K_\pi k_e[\text{XPhO}^-][\text{4NM}] \qquad (17)$$

so that $K_\pi k_e = k_2$ and the ratio of nitrated phenol to nitrite ion is provided by $k_a : k_b$. The inability to detect free-radical intermediates in water is also accounted for by Scheme I. The change in kinetic order from first to second order in *p*-cresol on going form water to ethanol and the second-order dependence of the rate on *t*-butylphenol in ethanol can be rationalized *via* formation of 2:1 complexes in ethanol and 1:1 complexes in water.

The formation of nitrite ion from tetranitromethane in a reaction in which both trinitromethane anion and a proton are released shows that estimation of the latter two products does not provide a measure of the yield of nitrophenol. Because of absorption by trinitromethane ion the absorbances at the $\lambda_{\max}$ of the nitrophenols also are not good measures of the extent of nitration, unless the trinitromethane anion is removed. These words are provided as a cautionary phrase to those who are employing 4NM in the modification of proteins.

Acknowledgments. This work was supported by grants from the National Science Foundation and the National Institutes of Health.

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[22] N. Kornblum, *Trans. N. Y. Acad. Sci.*, **29**, 1 (1966).

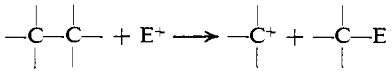
Oxidative Cleavage of Cyclopropanes. IV. Kinetics of the Cleavage of Arylcyclopropanes by Mercuric Acetate[1,2]

Robert J. Ouellette, Richard D. Robins, and Aubrey South, Jr.

Contribution from the Evans Chemical Laboratory, The Ohio State University, Columbus, Ohio 43210. *Received September 1, 1967*

Abstract: The kinetics of cleavage of six arylcyclopropanes by mercuric acetate in acetic acid have been examined. The reaction is over-all second order, first order in each reactant. Activation parameters have been determined from the rates of the reactions at 25, 50, and 75°. Electron-releasing substituents facilitate the reaction. A correlation of the second-order rate constants and σ^+ has been obtained for the substituents *p*-MeO, *p*-Me, *m*-Me, H, *p*-Cl, and *m*-Cl with $\rho = -3.2$ at 50°. Under the reaction conditions the phenylcyclopropane–mercuric acetate adduct is stable. For the slow reactions, with electron-withdrawing substituents on the aryl ring, a side reaction of mercuric acetate leads to some analytical complications. Initial rate studies and the use of excess concentrations of cyclopropanes allow the circumvention of this difficulty. The cleavage reaction is postulated to involve electrophilic attack of mercuric acetate on the cyclopropane ring. There are similarities between the cleavage of cyclopropanes and the oxymercuration of olefins.

The cleavage of a carbon–carbon single bond as the result of a direct bimolecular reaction with an electrophile is fundamentally a simple reaction. Such an attack is designated SE2 in the Hughes–Ingold terminology. In this type of reaction the electrophilic reagent may be thought to displace a carbonium ion. Of the many possible combinations of electrophiles and leaving groups that can be envisaged as participants in SE2 processes, only electrophilic attack on carbon–metal bonds has been examined in any detail. The only case where carbon–carbon single bonds are cleaved by electrophilic reagents is in compounds containing a cyclopropane ring.



$$-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}- + E^+ \longrightarrow -\overset{|}{\underset{|}{C}}{}^+ + -\overset{|}{\underset{|}{C}}-E$$

Cyclopropane ring cleavage by reagents, now classified as electrophiles, to yield adducts has been known since the 19th century.[3] The cleavage process can be interpreted in terms of initial electrophilic attack to produce an intermediate of carbonium ion like character followed by addition of a nucleophile. The degree of synchronization of attack by the electrophile and the nucleophile is a subject of some interest. In general the direction of cyclopropane ring cleavage is thought to reflect the stability of the incipient carbonium ion.[4] Most early investigations dealt with the problem of position of ring cleavage as a function of substitution. It has been generalized that Markovnikov's rule can be applied to the reactions of cyclopropanes as well as of olefins. However, the generalization clearly has to be modified to include the effect of other factors, such as ring strain and steric accessibility to the reagent. Of these two factors only ring strain has been examined in detail. In a thorough study of the acid-catalyzed addition of acetic acid to bicyclo[*n*.1.0]alkanes LaLonde[5]

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(1) Paper III: R. J. Ouellette, A. South, Jr., and D. L. Shaw, *J. Amer. Chem. Soc.*, **87**, 2602 (1965).

(2) This research was supported by Grant GP3873 from the National Science Foundation.

(3) A. Baeyer, *Chem. Ber.*, **18**, 2277 (1855); R. Fitlig and F. Roder, *Ann.*, **227**, 13 (1885); G. Gustauson, *J. Prakt. Chem.*, [2] **36**, 300 (1887).

(4) R. A. Raphael, "Chemistry of Carbon Compounds," Vol. II, E. H. Rodd, Ed., Elsevier Publishing Co., New York, N. Y., 1953, p 26; E. E. Royals, "Advanced Organic Chemistry," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1954, Chapter 3.

(5) R. T. LaLonde and L. S. Ferney, *J. Amer. Chem. Soc.*, **86**, 3767