

## ORGANIC AND BIOLOGICAL CHEMISTRY

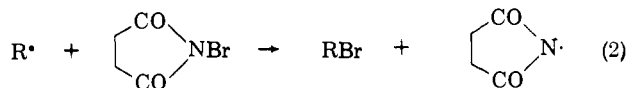
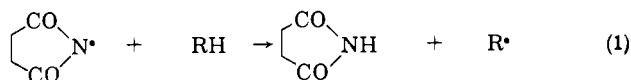
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY, NEW YORK 27, N. Y.]

Positive Halogen Compounds. VIII. Structure and Reactivity in N-Bromosuccinimide Brominations<sup>1</sup>BY CHEVES WALLING, ANNE L. RIEGER,<sup>2</sup> AND DENNIS D. TANNER

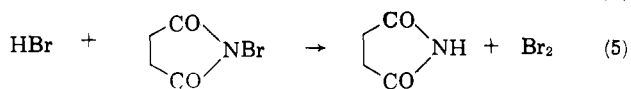
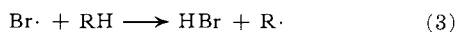
RECEIVED MARCH 23, 1963

Relative reactivities of a variety of hydrocarbons toward N-bromosuccinimide (NBS) have been compared in CCl<sub>4</sub> (heterogeneous system) at 80°; NBS is found to be highly selective, relative reactivities per H, toluene = 1, range from <0.01 for *sec*-aliphatic hydrogen to 50–100 for allylic hydrogens. Relative reactivities of substituted toluenes correlate well with  $\sigma^+$ -constants and yield  $\rho = -1.38$ . Olefins without reactive allylic hydrogen retard NBS bromination without significant reaction or change in relative reactivities. Dichloroethylene undergoes *trans-cis* isomerization, and styrene inhibits bromination entirely under our conditions. Our results agree with other recent work in supporting the conclusion that NBS and Br<sub>2</sub> reactions show such similar selectivity that a bromine atom chain is the most plausible mechanism for the NBS reaction and also suggest an explanation for some peculiarities of the NBS- $\beta$ -bromopropionyl isocyanate rearrangement.

The utility of N-bromosuccinimide (NBS) as a reagent for allylic bromination was first pointed out by Ziegler in 1942,<sup>3</sup> and a radical chain mechanism proposed for its action two years later by Bloomfield.<sup>4</sup> Since that time, in contrast to the literally hundreds of papers attesting to its widespread use and efficacy as a synthetic reagent, very little conclusive material has been published on the details of reaction mechanism.<sup>5</sup> Thus, although the radical chain nature of the reaction seems abundantly confirmed by examples of the catalytic effect of peroxides, other radical sources and ultraviolet light on the reaction, and the retarding properties of oxygen and other typical radical inhibitors,<sup>5</sup> to date there is still doubt as to the actual chain carriers. Bloomfield<sup>4</sup> originally suggested a chain-carrying sequence involving the succinimide radical which until recently has been accepted by most



workers. However, in 1953, Goldfinger<sup>6</sup> proposed an alternate scheme utilizing a bromine atom chain, made possible by the presence of traces of bromine or HBr in the reaction system



Here the NBS acts simply as a reservoir capable of sustaining a low steady-state concentration of bromine during the reaction. Tedder has recently espoused this scheme and has attempted to obtain further evidence in its support.<sup>7</sup> Very recently additional evidence for the bromine atom chain has been reported by Martin<sup>8</sup> and by Russell.<sup>9</sup> Finally, it should be

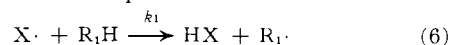
noted that, in 1952, Orazi and Corral actually proposed a more complex set of reactions in order to account for saturated dibromides accompanying allylic substitution, in which bromine atom and succinimide radical processes compete.<sup>10</sup>

One difficulty in carrying out mechanistic studies on NBS reactions is that kinetic studies are extraordinarily difficult. As usually conducted, NBS brominations are heterogeneous reactions due to the low solubility of NBS in organic solvents, and even in homogeneous systems reproducible rates are very difficult to achieve,<sup>11</sup> in part at least because of the extreme sensitivity of the reaction to a whole variety of possible impurities.<sup>11,12</sup> Further, quantitative yields of single products are rarely attained (side-chain bromination of aromatics being the most notable exception) and the instability of allylic bromides often leads to their extensive decomposition during reaction.

An alternate approach to the study of radical chain processes which avoids most of these difficulties is by investigation of the relative rates of reaction of different substrates with the chain-carrying radicals. Rather surprisingly, when our study was begun very few quantitative data of this sort were available for NBS. Kooyman<sup>13</sup> had studied the competitive bromination of a series of toluenes, but otherwise one had to be content with a few scattered observations on isomeric product distributions and the well established fact that allylic hydrogens are attacked in preference to those on purely aliphatic carbons. We accordingly undertook a systematic study of the relative reactivities of different substrates towards NBS, both to provide a better quantitative basis for predicting the products expected in its synthetic use, and to try to differentiate more conclusively between the different possible chain carriers in the reaction. The following paper<sup>14</sup> describes a similar study on some other haloimides and amides.

## Results of Competitive Experiments

**Hydrocarbons.**—In a radical chain halogenation where two substrates compete



(9) G. G. Russell, C. De Boer, and K. M. Desmond, *ibid.*, **85**, 365 (1963). We wish to acknowledge that Martin and Russell's results were made available to us prior to publication and led to revision of some of our tentative conclusions.

(10) H. J. Schumacher, O. O. Orazi, and R. A. Corral, *Anales asoc. quim. argentina*, **40**, 19 (1952).

(11) E. A. Youngman, Ph.D. Thesis, University of Washington, 1952.

(12) H. J. Dauben, Jr., and L. L. McCoy, *J. Am. Chem. Soc.*, **81**, 4863 (1959).

(13) E. C. Kooyman, R. Van Helden, and A. F. Bickel, *Koninkl. Ned. Akad. Wetenschappen Proc.*, **B56**, 75 (1953).

(14) C. Walling and A. L. Rieger, *J. Am. Chem. Soc.*, **85**, 3134 (1963).

(1) Taken in part from the Ph.D. Dissertation of Anne L. Rieger, Columbia University, 1962. Support of this work by a grant from the National Science Foundation is gratefully acknowledged.

(2) Socony Mobil Oil Co. Fellow, 1960–1961.

(3) K. Ziegler, A. Spaeta, E. Schaaf, W. Schumann, and E. Winkelmann, *Ann.*, **551**, 80 (1942).

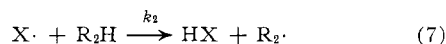
(4) C. F. Bloomfield, *J. Chem. Soc.*, 14 (1944).

(5) For a summary of evidence, cf. C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, pp. 381–386.

(6) J. Adam, P. A. Gosselain, and P. Goldfinger, *Nature*, **171**, 704 (1953); *Bull. soc. chim. Belges*, **65**, 533 (1956).

(7) B. P. McGrath and J. M. Tedder, *Proc. Chem. Soc.*, 1511 (1961).

(8) R. E. Pearson and J. C. Martin, *J. Am. Chem. Soc.*, **85**, 354 (1963).



The ratio of rate constants may be computed from the relation

$$\log ([R_1H]_0/[R_1H]) / \log ([R_2H]_0/[R_2H]) = k_1/k_2 \quad (8)$$

If a deficiency of halogenating agent is used so that significant quantities of both substrate remain at the end of the reaction,  $[R_1H]$  and  $[R_2H]$  may either be determined directly or calculated from the yields of  $R_1X$  and  $R_2X$  obtained. The former method has the advantage that it avoids any difficulties owing to polyhalogenation or product instability and was used in the work reported here.

In the case that the two substrates differ too much in reactivity for accurate measurement of the quantities in eq. 8, rate constant ratios may be obtained by successive comparisons with substrates of intermediate reactivity. Results of such competitive NBS brominations of an extensive series of hydrocarbons are listed in Table I. Analyses were by gas-liquid chromatog-

TABLE I  
RELATIVE REACTIVITY OF HYDROCARBONS TOWARD NBS<sup>a</sup>

Hydrocarbon	Rel. react.		No. expt.
	Per molecule	Per H <sup>a</sup>	
Cyclohexene	172 ± 30	129 ± 22	4
Cyclopentene	132 ± 18	99 ± 15	2
2-Methyl-2-butene	227 ± 36	76 ± 12	2
sec-Butylbenzene	20.4 ± 3	61 ± 9	2
Cumene	16.0 ± 2.7	50 ± 7	3
Isoprene	48 ± 7	48 ± 7	2
1-Octene	26.4 ± 4	40 ± 6	4 <sup>b</sup>
1-Pentene	23.5 ± 4	35.6 ± 6	2
1-Hexene	23.2 ± 3	35 ± 4	2
n-Butylbenzene	19 ± 3	28.5 ± 4	4
Tetralin	34.6 ± 5.4	25.3 ± 4	2
Ethylbenzene	15.8 ± 2.1	23.6 ± 3.3	5 <sup>b</sup>
n-Propylbenzene	18.8 ± 1.3	28.2 ± 2.0	4
Toluene (std.)	1.00	1.00	..
2,3-Dimethylbutane	0.070 ± 0.004	0.105 ± 0.006	2 <sup>c</sup>
Methylcyclohexane	.027 ± .002	.071 ± .006 <sup>d</sup>	4 <sup>e</sup>
n-Hexane	.025 ± .0019	.0095 ± .0007	8
n-Octane	.0216 ± .0016	.0054 ± .0004	2
Cyclohexane	.0116 ± .0008	.0028 ± .0002	2

<sup>a</sup> Assuming only most reactive hydrogens are attacked in order 2° < 3° < benzylic < allylic. <sup>b</sup> Including two reactions in benzene as solvent. <sup>c</sup> No solvent. <sup>d</sup> Corrected for 2° hydrogens. <sup>e</sup> At 80° in CCl<sub>4</sub>; azobisisobutyronitrile initiator unless indicated.

raphy (g.l.c.) using internal standards essentially as in previous papers from this Laboratory,<sup>15-17</sup> and experimental errors represent average deviations from the mean of 2-8 experiments. The major uncertainty in the results, aside from irreproducibility of the analyses, is the possibility that the hydrocarbons were consumed by processes other than hydrogen abstraction. For the alkylbenzenes nuclear substitution was ruled out by examining the g.l.c. traces for such products, while for the saturated alkanes no such competing process appears possible. The situation with the olefins is somewhat less certain, since some competing addition of bromine to the double bond is entirely possible. However, allylic bromides are well established as the major products in such NBS reactions, and our material balances show substrate consumptions approaching 1 mole/mole NBS consumed. Considering that some

polysubstitution is undoubtedly taking place and that some NBS probably disappears *via* conversion to β-bromopropionyl isocyanate (see below), we are confident that the large differences in reactivities noted are real, even though here some uncertainties may be greater than the experimental errors shown, particularly where a sequence of indirect comparisons are involved.

The most significant features of Table I are the very high selectivity of the NBS reaction, with an over-all sequence of substrate hydrogen reactivity of paraffinic < benzylic < allylic. This is shown up more clearly in Table II where relative reactivities of different C-H bonds are compared for the three most extensively studied radical halogenating species: chlorine, *t*-butyl hypochlorite, and NBS.

TABLE II  
COMPARISON OF RADICAL HALOGENATING AGENTS<sup>c</sup>

	Reagent		
	Cl <sub>2</sub> (40°)	C <sub>4</sub> H <sub>9</sub> OCl (40°)	NBS (80°)
Cyclohexene	..	36.4 <sup>17</sup>	129
1-Pentene	..	6.05 <sup>a,17</sup>	35.6
Cumene	4.0 <sup>b,18</sup>	6.84 <sup>16</sup>	50
Ethylbenzene	..	3.18 <sup>16</sup>	23.6
Toluene (std.)	1.00	1.00	1.00
2,3-Dimethylbutane	3.4 <sup>19</sup>	4.20 <sup>16</sup>	0.105
Cyclohexane	2.3 <sup>19</sup>	1.50 <sup>16</sup>	0.0028

<sup>a</sup> Value is actually for 1-butene. <sup>b</sup> 80°.

The less extensive data on bromine will be considered later in connection with our discussion of the nature of the chain carrier in the NBS reaction. Data for chlorine are in largely aliphatic media, to minimize any solvent effects.<sup>19</sup> Solvent effects on selectivity appear to be minor with *t*-butyl hypochlorite,<sup>14</sup> and competitions between toluene and ethylbenzene in NBS bromination yield indistinguishable results in CCl<sub>4</sub> and benzene.

From the tables it is evident that NBS is enormously more selective for benzylic hydrogens compared with aliphatic hydrogens than is either chlorine or *t*-butyl hypochlorite, and is certainly the reagent of choice when such selectivity is desired in the halogenation of complex molecules. When allylic substitution is desired, chlorine is unsuitable, both because of its low selectivity and its tendency to add to double bonds, and the choice is between the hypochlorite and NBS (or other N-halo compounds, discussed in the following paper). Again NBS offers the greatest selectivity where this is important, for example, in a complex molecule with a large number of aliphatic hydrogens. On the other hand, *t*-butyl hypochlorite permits reaction in homogeneous systems at low temperatures, and yields relatively stable allylic chlorides. It is also doubtful that one can observe the *cis-trans* stereospecificity of reaction of *t*-butyl hypochlorite<sup>17</sup> with NBS, or the formation of kinetically controlled ratios of allylic isomers, due to the very facile isomerization of allylic bromides in the presence of free radicals.

Finally, we see that relative reactivities of hydrocarbons toward NBS appear to increase regularly with decrease in strength of the C-H bond being attacked, except that allylic bonds are in general more reactive than benzylic. The order of reactivity of different allylic bonds parallels that observed with *t*-butyl hypochlorite, including the markedly enhanced reactivity of allylic hydrogens in systems with endocyclic double bonds (cyclopentene and cyclohexene). On the other hand, although Szwarc<sup>20</sup> has recently

(15) C. Walling and W. Helmreich, *J. Am. Chem. Soc.*, **81**, 1144 (1959).

(16) C. Walling and B. B. Jacknow, *ibid.*, **82**, 6108 (1960).

(17) C. Walling and W. Thaler, *ibid.*, **83**, 3877 (1961).

(18) G. A. Russell and H. C. Brown, *ibid.*, **77**, 4578 (1955).

(19) G. A. Russell, *ibid.*, **80**, 4997 (1958).

(20) J. A. Meyer, V. Stannett, and M. Szwarc, *ibid.*, **83**, 25 (1961).

pointed out the abnormally high reactivity of the benzylic hydrogens of tetralin toward radical attack in several systems, the phenomenon appears to be lacking in the NBS reaction, tetralin hydrogens showing essentially the same reactivity as those of ethyl-, *n*-propyl-, and *n*-butylbenzene.

**Substituted Toluenes.**—In 1953, Kooyman investigated the relative reactivities of a series of substituted toluenes toward NBS, and reported that his results showed a linear Hammett  $\rho\sigma$  relation corresponding to  $\rho = -1.55$ .<sup>13</sup> Jaffé, using a revised set of constants, has indicated that  $\rho = -1.81$  is a better value,<sup>21</sup> and Russell<sup>22</sup> has suggested that a better fit is obtained using the  $\sigma^+$ -values of Okamoto and Brown<sup>23</sup> for the substituents. The choice is difficult, since Kooyman's results were chiefly for negatively substituted toluenes where  $\sigma^-$  and  $\sigma^+$ -constants do not differ greatly. Since the question was of some interest, we extended Kooyman's series to a number of other substituted toluenes. Our results, together with those in the literature, appear in Table III.

TABLE III  
RELATIVE REACTIVITIES OF SUBSTITUTED TOLUENES TOWARD NBS<sup>a</sup> (PER H) AT 80° IN CCl<sub>4</sub>

Substituent	Rel. react. NBS	Substituent	Rel. react. NBS
<i>p</i> -OCH <sub>3</sub>	11.7 ± 0.7 (3)	<i>p</i> -F	0.58 ± 0.02 (4)
	9.0 <sup>11</sup>	<i>m</i> -COOH	.30 <sup>11</sup>
<i>p</i> -CH <sub>3</sub>	2.56 ± 0.17 (3)	<i>p</i> -COOH	.22 <sup>11</sup>
<i>p</i> - <i>t</i> -C <sub>4</sub> H <sub>9</sub>	2.0 <sup>11</sup>	<i>m</i> -Br	.24 <sup>11</sup>
<i>m</i> -CH <sub>3</sub>	1.52 ± 0.05 (4)	<i>p</i> -CN	.14 <sup>11</sup>
H (std.)	1.00	<i>m</i> -CN	.11 <sup>11</sup>
<i>m</i> -OCH <sub>3</sub>	0.75 <sup>11</sup>	<i>m</i> -NO <sub>2</sub>	.08 <sup>11</sup>
<i>p</i> -Br	.94 ± 0.03 (2)	<i>p</i> -NO <sub>2</sub>	.05 <sup>11</sup>
<i>p</i> -Cl	.80 ± .02 (4) <sup>b</sup>		.11 <sup>24</sup>

<sup>a</sup> Our results unless indicated; numbers in parentheses show number of independent experiments. <sup>b</sup> Including two runs in benzene as solvent.

In Fig. 1 data are plotted against both  $\sigma^-$  and  $\sigma^+$ -values for the substituents, using our value for *p*-methoxytoluene, and that of Sixma and Riem<sup>24</sup> for *p*-nitrotoluene since they indicate high reproducibility in their experiments. The superiority of the  $\sigma^+$  fit is now quite evident, and indicates  $\rho = 1.38$  with a correlation coefficient  $r = 0.977$  and a standard deviation  $s = 0.041$ . This value agrees well with Martin's<sup>8</sup> recent value in benzene at 80°,  $\rho = -1.46$  with a standard deviation of 0.07, indicating no aromatic solvent effect on the reaction.

The correlation with  $\sigma^+$ -values points in Russell's terms<sup>22</sup> to a strongly electron-accepting radical forming only weak radical hydrogen bonds so that bond breaking is extensive in the transition states, and charge transfer structures make an important contribution to their stability. Such a result is certainly consistent with the high selectivity of NBS between C-H bonds of different strengths shown in Tables I and II.

**The Nature of the Chain-Carrying Radical in NBS Bromination.**—We now turn to the question whether our results, together with those in the literature, permit a decision as to the nature of the chain carrier in NBS brominations: specifically the relative roles of succinimide radical and bromine atom—reactions 1-2 and 3-5, respectively—since we accept as convincing the general evidence of the radical chain nature of the reaction.

(21) H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953).

(22) G. A. Russell, *J. Org. Chem.*, **23**, 1407 (1958).

(23) H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **80**, 4979 (1958).

(24) F. L. J. Sixma and R. H. Riem, *Koninkl. Ned. Akad. Wetenschappen Proc.*, **B61**, 183 (1958).

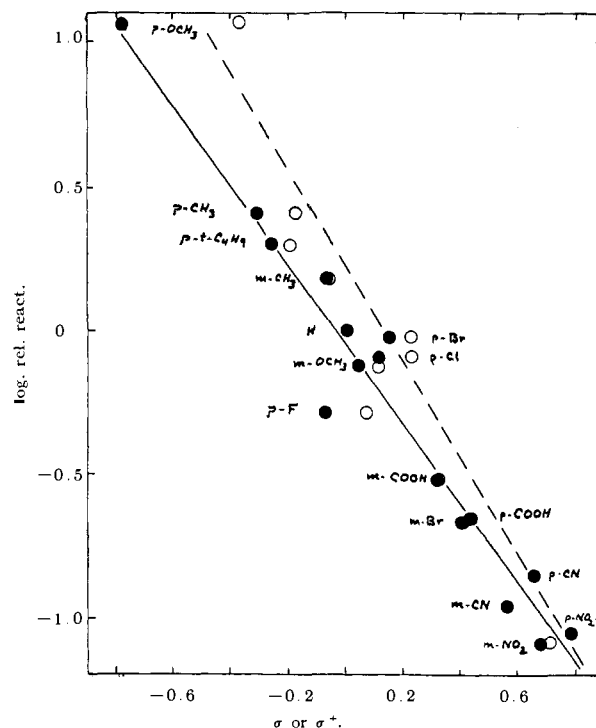
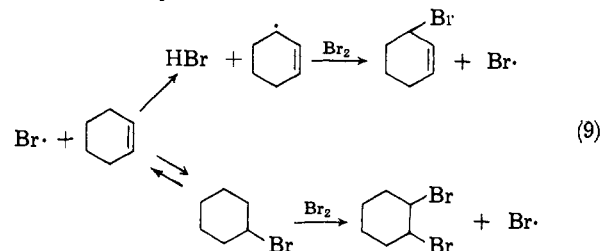


Fig. 1.—Hammett  $\rho\sigma$  correlation for NBS bromination of substituted toluenes: black circles, solid line,  $\sigma^+$ -correlation,  $\rho = -1.38$ ,  $r = 0.977$ ,  $s = 0.041$ ; open circles, dashed line,  $\sigma^-$ -correlation,  $\rho = -1.68$ ,  $r = 0.945$ ,  $s = 0.198$ . Where  $\sigma^-$  and  $\sigma^+$  are identical for a substituent, only  $\sigma^+$  is shown.

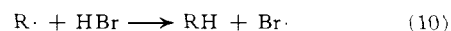
The chief pieces of evidence available are over-all kinetics, relative reactivity data, and the  $\beta$ -bromopropionyl isocyanate rearrangement, but, before considering them, we must point out certain complexities in the bromine atom process.

In the Goldfinger scheme,<sup>6</sup> using cyclohexene as a model, allylic substitution rather than addition of bromine to the double bond is accounted for on the basis of the competition



If the addition step is reversible, low bromine concentrations will favor the hydrogen abstraction process. Extensive evidence exists for the easy reversibility of bromine atom additions near room temperature, *e.g.*, rapid *cis-trans* isomerization of olefins and equilibration of allylic bromides in the presence of bromine atoms.<sup>25</sup> In fact, both Sixma and Riem<sup>24</sup> and also McGrath and Tedder<sup>7</sup> have shown that very slow photoaddition of bromine to cyclohexene gives 3-bromocyclohexene in good yield, and Tedder has adduced the presence of bromine atoms during the reaction of NBS with *cis*-3-hexene by showing that unreacted olefin is largely isomerized to *trans*-3-hexene.<sup>7</sup>

Actually the hydrogen abstraction step in bromination is also reversible and reaction 10) is a well recog-



nized step in the "abnormal" (radical) addition of HBr to olefins. The significance of this reversibility in

(25) For discussion and references, *cf.* ref. 5, pp. 302-308.

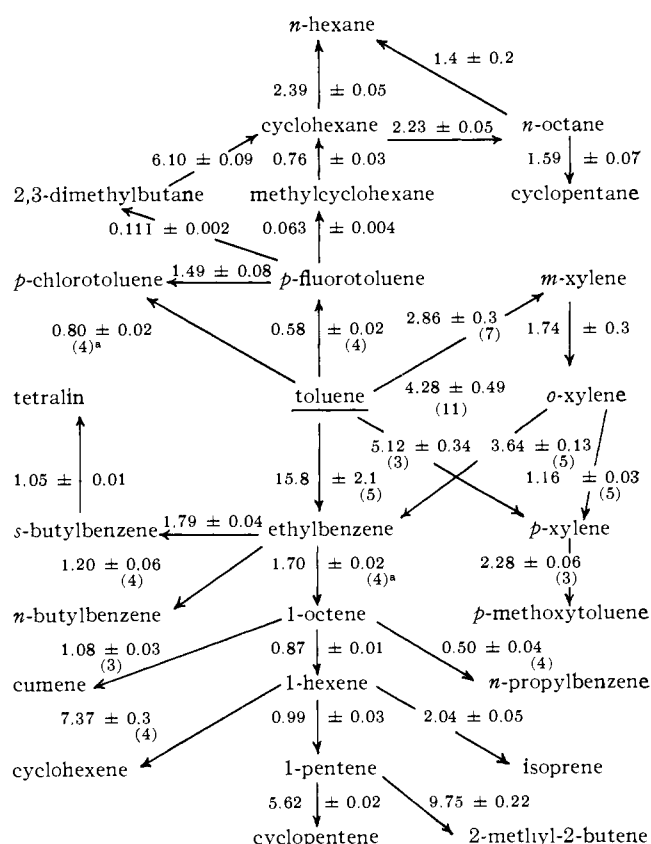
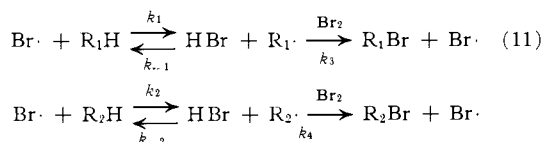


Fig. 2.—Summary of competitive NBS brominations, all at 80° in CCl<sub>4</sub> unless indicated (\* indicates inclusion of two experiments in benzene). Arrows indicate direct competitions; numbers are relative reactivities per molecule at head of arrow to that at tail. All experiments in duplicate unless a larger number is given in parentheses.

brominations has perhaps not been adequately appreciated, although the HBr inhibition of bromination has been demonstrated kinetically, *e.g.*, for toluene in the gas phase.<sup>26</sup> and Wiberg<sup>27</sup> has shown that, in measuring the kinetic isotope effect  $k_H/k_D$  in toluene bromination, low and erratic values were obtained unless HBr was continuously removed from the system.

If such reversibility is serious, relative reactivities in competitive reactions involving bromine are not determined by an expression such as 8, but are the result of a more complex sequence of reactions



yielding the relation

$$\frac{d \ln [R_1H]}{d \ln [R_2H]} = \frac{k_1}{k_2} \frac{1 + k_{-2}[HBr]/k_4[Br_2]}{1 + k_{-1}[HBr]/k_3[Br_2]} \quad (12)$$

Unfortunately, this predicted dependence of  $d \ln [R_1H]/d \ln [R_2H]$  on the  $[HBr]/[Br_2]$  ratio has not been determined for relative reactivities which have been reported for bromine. For NBS processes we shall assume that, if a Br· chain is involved, the ratio is vanishingly small due to the high rate of reaction 5.

Considering now the NBS problem, the only detailed kinetic study of which we are aware<sup>11</sup> has shown that with cyclohexene, initiated by azobisisobutyronitrile (AIBN), the reaction follows the law  $-d[NBS]/$

$dt = k[RH][AIBN]^{1/2}$ . This result is consistent with a succinimide radical chain and chain termination *via* two succinimide radicals. It is also easy to show that it is consistent with a bromine atom chain and termination *via* two bromine atoms, although it is perhaps surprising that this type of termination would be observed at the very low bromine concentrations postulated for the bromine atom scheme.

As we have seen, our relative reactivity data for NBS reactions with substituted toluenes correlate with  $\sigma^+$ -constants and yield  $\rho = -1.38$ . This value is significantly different from the results with Br<sub>2</sub> reported by Kooyma,<sup>13</sup> whose data also correlate with  $\sigma^+$ -constants but indicate  $\rho = -1.07$ . However, Martin's recent results,<sup>8</sup> obtained at high  $[Br_2]/[HBr]$  ratios to minimize the reverse reaction (10), yield  $\rho = -1.36$  very close to his own value for NBS ( $\rho = -1.46$ ) and our own.

It is difficult to find many other systems where clean competitive brominations can be carried out with both Br<sub>2</sub> and NBS, but Table IV lists some values for cyclohexane and alkylbenzenes. Our experiments were in sealed tubes so HBr was present; Russell<sup>9</sup> states that removal of HBr had no effect.<sup>28</sup>

TABLE IV  
RELATIVE REACTIVITIES IN NBS AND Br<sub>2</sub> REACTIONS<sup>a</sup>

	NBS	Br <sub>2</sub>
Cyclohexane	0.012	0.017 <sup>18</sup>
Toluene (std.)	1.00	1.00
Ethylbenzene	15.8 ± 2.1	8.5 ± 0.02 (2)
	8.3 ± 1 (4) <sup>b</sup>	
	14 ± 2 <sup>9</sup>	11 ± 2 <sup>9</sup>
Cumene	14 ± 2 <sup>9</sup>	12 ± 1 <sup>9</sup>
Diphenylmethane	7 ± 1 <sup>9</sup>	7 ± 1 <sup>9</sup>

<sup>a</sup> Our data in CCl<sub>4</sub> at 80° unless indicated; number of experiments in parentheses. <sup>b</sup> In presence of 6% added Br<sub>2</sub>.

The data of Table IV and the results with substituted toluenes are consistent in that Br<sub>2</sub> and NBS reactions show very similar properties, but Table IV suggests a slightly higher selectivity for NBS. Wiberg and Slauch<sup>27</sup> came to a similar conclusion on determining  $k_H/k_D$  ratios for toluene ( $4.59 \pm 0.03$  for Br<sub>2</sub> and  $4.86 \pm 0.03$  for NBS). If these differences are real, competitive bromination data leave us with two alternative hypotheses. NBS reactions can occur at least in part through succinimide radical chains, but succinimide radicals and bromine atoms have almost but not quite identical selectivities. Alternatively, bromine atoms are the chain carriers in both reactions, but selectivities in Br<sub>2</sub> reactions may be reduced by kinetic complications due to reversibility.

Additional observations favor the second hypothesis, which we consider the more plausible. Qualitatively, competitive NBS brominations involving olefins undergo reaction more slowly than those employing only alkylbenzenes. A possible explanation involving the bromine atom chain is that here competing bromine atom addition removes bromine atoms without regenerating HBr. Consistent with this conclusion, we find that small amounts of olefins without reactive allylic hydrogens, allyl bromide and dichloroethylene, also retard the NBS bromination of alkylbenzenes without themselves undergoing significant reaction (*trans*-dichloroethylene is, however, isomerized to *cis*). Furthermore, small amounts of the more reactive olefin styrene completely suppress the bromination of

(26) H. R. Anderson, H. A. Scheraga, and E. R. Van Artsdalen, *J. Chem. Phys.*, **21**, 1258 (1953).

(27) K. B. Wiberg and L. H. Slauch, *J. Am. Chem. Soc.*, **80**, 3033 (1958).

(28) The reasonable agreement between Russell's results in homogeneous solution and ours in a heterogeneous system are strong evidence against any significant difference in mechanism in the two cases as suggested by L. Horner and E. H. Winkelmann, *Angew. Chem.*, **71**, 349 (1959).

alkylbenzenes initiated by a small amount of AIBN, although the styrene is again not consumed.<sup>29</sup>

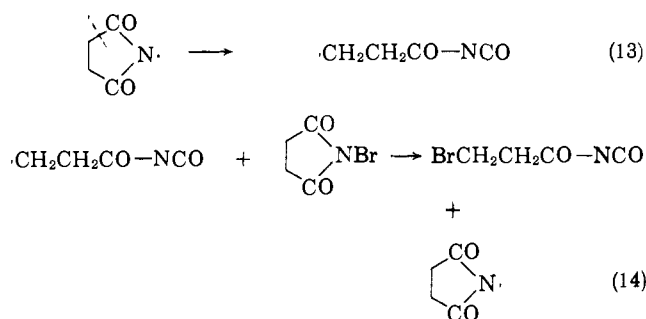
If these olefins act by removing bromine atoms, their presence should favor a succinimide radical chain if such is possible. We have examined their effect on the three-way competitive bromination of toluene-*o*-xylene-ethylbenzene; Table V. We see no significant trend lying beyond experimental error.

TABLE V  
EFFECT OF OLEFINS ON COMPETITIVE NBS REACTIONS

	Rel. react.		
	None	<i>trans</i> -C <sub>2</sub> H <sub>2</sub> Cl <sub>2</sub>	Allyl bromide
Toluene	1.00	1.00	1.00
<i>o</i> -Xylene	4.28 ± 0.49(11)	4.84 ± 0.29(5)	4.72 ± 1.2(7)
Ethylbenzene	15.8 ± 2.1(5)	18.8 ± 1.08(5)	14.9 ± 3.2(7)

Even though our data thus provide no evidence for succinimide radical participation in the NBS bromination chain, it is entirely possible that succinimide radicals are formed reversibly during the reaction, *e.g.*, by radical attack on NBS, followed by reaction of the succinimide radical with Br<sub>2</sub>. Their presence is certainly suggested by the occasional report of NBS addition products to olefins during halogenation, and also by the occurrence of the NBS- $\beta$ -bromopropionyl isocyanate rearrangement.

This reaction, discovered independently by Bartlett and Martin<sup>30</sup> and Johnson and Bublitz,<sup>31</sup> evidently arises from a competing radical chain, since it requires the presence of radical sources. The most plausible formulation<sup>30</sup> is certainly the sequence



Bartlett and Martin obtained the isocyanate by refluxing NBS in CCl<sub>4</sub>, but Johnson and Bublitz reported that the presence of chloroform and an olefin (usually allyl chloride or bromide) were required for the reaction. We have been able to detect the isocyanate, either by infrared spectra or in some cases simply by its characteristic odor, as a product of NBS reactions run under a variety of conditions. However, no simple inverse relation between substrate reactivity and yield was discernible from our results, and our best yield (54% as the corresponding methylcarbamate) was also obtained in chloroform containing a little allyl chloride.

If allyl chloride is acting as a bromine atom trap, such results are comprehensible, since it suppresses consumption of NBS *via* normal bromination of chloroform which would be at best a slow process.

An alternative or parallel explanation is suggested by results of another investigation in this Laboratory. Walling and Padwa<sup>32</sup> have shown that with alkoxy radicals, notably the benzylidimethylmethoxy radical, the competition between hydrogen abstraction from

substrates such as cyclohexane and  $\beta$ -scission is shifted entirely toward scission in the presence of small amounts of olefin and have interpreted the result essentially as a solvent effect. They further point out that solvation of the transition states of unimolecular radical decompositions should usually be favored for steric reasons over solvation of transition states for radical-substrate reactions. If succinimide radical-olefin interaction occurs, the  $\beta$ -scission (13) should be similarly favored over, for example, reaction of the succinimide radical with bromine, and the rearrangement facilitated.

In either case, a bromine atom chain for bromination and a succinimide radical chain for the rearrangement do not appear incompatible, and we reach the conclusion that radicals may attack NBS<sup>33</sup> but that the succinimide radical is too unreactive to attack C-H bonds. The N-H bond dissociation energy of succinimide has been estimated as 74 kcal.,<sup>12</sup> which would make such hydrogen abstractions endothermic, and it is perhaps significant that N-iodosuccinimide is reported to be ineffective as a free radical halogenating agent.<sup>34</sup> Here the succinimide radical chain, were it possible, should be easily realized, but an iodine atom chain is energetically prohibited.

### Experimental

**Materials.**—Hydrocarbons, solvents, and substituted toluenes were commercial materials. Before use they were distilled, physical constants determined, and purity checked by g.l.c. NBS was supplied by Dr. Thomas Waugh of Arapahoe Chemicals, Inc. It was purified by rapid recrystallization from boiling distilled water as recommended by McCoy,<sup>35</sup> purity 99.8–100.1% by iodometric titration.<sup>36</sup> Different batches gave identical results.

**Competitive Brominations.**—Preliminary experiments using dilute homogeneous systems in methylene chloride were found to give erratic results, so all experiments reported here were carried out in heterogeneous systems consisting of substrates, solvent (usually CCl<sub>4</sub>), NBS, inert internal standard for g.l.c. analysis (chlorobenzene, bromobenzene, or halogenated alkane), and azobisisobutyronitrile as initiator. These are essentially the conditions under which NBS is used synthetically. Individual experiments were made up by weighing NBS into small tubes, adding aliquots of a standard solution of substrates and internal standard and of initiator, degassing under vacuum, sealing, and storing below 0° until used. A typical reaction mixture would contain 3 mmoles of NBS, 1.5–4 moles each of two hydrocarbons, 1 mmole of internal standard, and 0.03 mmole of initiator in a total volume of 3 ml. Reactions were carried out with mechanical shaking in a thermostat at 80°, and were usually complete in under 3 hr. The tubes were then cooled, opened, and worked up either by distilling under vacuum into a liquid N<sub>2</sub> trap, or (better) by simply decanting the liquid from residual insoluble succinimide; g.l.c. analyses were carried out in triplicate, comparing peak areas before and after reaction with that of the internal standard as in previous work<sup>13–15</sup> in this Laboratory.

**Calculation of Relative Reactivities.**—Relative reactivities were calculated *via* eq. 8, either directly, or, where substrates differed markedly in reactivity, by stepwise comparison of suitable pairs. Thus all highly reactive molecules were related to toluene *via* ethylbenzene, and unreactive ones *via* *p*-fluorotoluene. The actual comparisons employed are shown in Fig. 2. Experimental errors are average deviations from the mean and when successive comparisons were required to give the results in Tables I–III the usual formula for propagation of errors was employed.<sup>37</sup> Although our analytical method involved disappearance of substrates rather than appearance of product, the assumption that displacement was the predominant reaction in every case seems quite justified. In all toluene brominations g.l.c. traces were examined for nuclear substitution with negative results. Material balances between NBS reacted and hydrocarbon consumed were also good. Hydrocarbon consumption

(33) Reaction of phenyl- and 2-cyano-2-propyl radicals with NBS gives bromobenzene and  $\alpha$ -bromoisobutyronitrile, respectively, in good yield; M. C. Ford and W. A. Waters, *J. Chem. Soc.*, 2240 (1952); M. C. Ford, *ibid.*, 2529 (1955).

(34) C. Djerassi and C. T. Lenk, *J. Am. Chem. Soc.*, **75**, 3494 (1953).

(35) L. McCoy, Thesis, University of Washington, 1951.

(36) T. Waugh, "NBS, Its Reactions and Uses," Arapahoe Chemicals, Inc., 1951.

(37) For further details of individual experiments, g.l.c. techniques, etc., *cf.* A. L. Rieger, Thesis, Columbia University, 1962.

(29) M. S. Kharasch and H. M. Priestley, *J. Am. Chem. Soc.*, **61**, 3425 (1939), report only a 6% yield of dibromide on prolonged reaction of styrene and NBS. *Cf.* also W. J. Bailey and J. Bello, *J. Org. Chem.*, **20**, 525 (1955).

(30) J. C. Martin and P. D. Bartlett, *J. Am. Chem. Soc.*, **79**, 2533 (1957).

(31) H. W. Johnson, Jr., and D. E. Bublitz, *ibid.*, **79**, 753 (1957); **80**, 3150 (1958).

(32) C. Walling and A. Padwa, *ibid.*, **84**, 2845 (1962); **85**, 1593 (1963).

averaging 93% of NBS reacted with the toluene experiments and 86% in the other systems. Considering that some polybromination and NBS decomposition to  $\beta$ -bromopropionyl isocyanate must be occurring, the agreement is very satisfactory.

**Bromine Reactions.**—The data of Table IV were obtained by direct competition reactions, essentially as in the case of NBS; relative reactivities (per molecule), ethylbenzene:toluene, 8.70, 8.27. The competitive bromination of ethylbenzene and toluene by NBS in the presence of 6 mole % added bromine was also carried out directly: relative reactivity per molecule, ethylbenzene:toluene 7.74, 7.79, 10.21, 8.24.

**Detection of  $\beta$ -Bromopropionyl Isocyanate.**—Decomposition of 0.1 mole of NBS in dry refluxing chloroform in the presence of 2 mole % benzoyl peroxide and 10 mole % allyl chloride gave a reaction mixture with an infrared spectra showing the peaks reported for  $\beta$ -bromopropionyl isocyanate.<sup>30</sup> Removal of solvent and treatment of the residue with methanol gave 11.3 g. of  $\beta$ -

bromopropionyl carbamate after recrystallization from methanol; m.p. 132–134.5 (lit.<sup>31</sup> 137–138°). The isocyanate was also detected by infrared spectra (but not determined quantitatively) in decompositions run in methylene chloride with and without allyl chloride, and its characteristic odor noted in other systems containing relatively unreactive substrates.

**NBS Reactions in Presence of Olefins.**—Typically 380 mg. of NBS and 0.320 ml. each of toluene, *o*-xylene, and ethylbenzene were allowed to react in the presence of 0.4 mg. of AIBN, 0.320 ml. of olefin, 2.60 ml. of  $\text{CCl}_4$ , and 0.320 ml. of chlorobenzene as an internal standard. Reactions took 90 min. for complete reaction as compared with 45 min. in the absence of olefin. Products were analyzed as before. Little olefin (0–10%) was consumed, but *trans*-dichloroethylene underwent 70–74% isomerization to *cis*. Similar experiments in the presence of either 0.320 or 0.032 ml. of styrene showed no significant reaction in 6 hr. at 80° at which time the initiator was essentially exhausted.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY, NEW YORK 27, N. Y.]

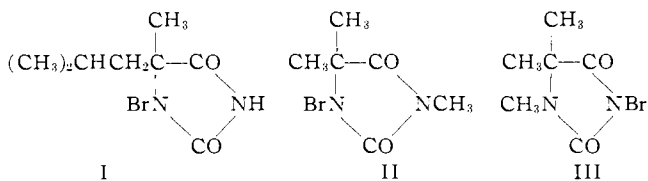
## Positive Halogen Compounds. IX. Structure and Reactivity in Halogenation with Some Further N-Haloamides<sup>1</sup>

BY CHEVES WALLING AND ANNE L. RIEGER<sup>2</sup>

RECEIVED MARCH 23, 1963

Relative reactivities of a series of hydrocarbons toward bromination with three N-bromohydantoins and N-bromoacetamide have been determined and compared with results from N-bromosuccinimide bromination. Relative reactivities for ethylbenzene:toluene are quite similar (6–15) and  $\rho$ -values for substituted toluenes appear within experimental error (–1.10 to –1.36). It is concluded that all reactions occur most probably through bromine atom chains. Relative reactivity of cyclohexane:toluene toward N-chlorosuccinimide is  $3.9 \pm 0.3$ , indicating a chlorine atom chain in this case.

Although they have attracted much less attention and received less use than N-bromosuccinimide (NBS), a number of other N-haloamides are known to act as effective halogenating agents for the replacement of allylic and benzylic hydrogen by what are quite evidently free radical chain processes. In particular, the series of N-bromohydantoins have been studied in some detail by Orazi,<sup>3</sup> and an allylic bromination by N-bromoacetamide (NBA) was reported as early as 1919 by Wohl.<sup>4</sup> It accordingly seemed worthwhile to extend our studies with NBS<sup>5</sup> to a series of other such N-haloamides, both to see whether differences in selectivity exist which would be of synthetic interest, and to identify if possible the chain carriers in the radical reactions involved. This paper reports an investigation of the reactions of 1-bromo-5-isobutyl-5-methylhydantoin (I), 1-bromo-3,5,5-trimethylhydantoin (II), 3-bromo-1,5,5-trimethylhydantoin (III), N-bromoacetamide (NBA), and N-chlorosuccinimide.



### Results and Discussion

**Substituted Toluenes.**—Relative reactivities of substituted toluenes toward the four N-bromoamides mentioned above were determined in  $\text{CCl}_4$  solution at 80°, using azobisisobutyronitrile as initiator, essentially as in our work with NBS, employing stepwise comparisons when compounds differed markedly in

reactivity. Results are summarized in Table I together with our NBS results.<sup>5</sup> Experimental errors are average deviation of the mean for duplicate experiments unless a larger number is indicated in parentheses. The Hammett  $\rho$ - $\sigma$  relation was investigated for each N-bromoamide, and it was found in every case (as with NBS) that  $\sigma^+$ -constants<sup>6</sup> gave a better correlation with the data than did  $\sigma$ -constants. Values of  $\rho$  and  $r$  (the correlation coefficient) and  $s$  (standard deviation from the regression line) are included in the table. The close similarity of  $\rho$ 's for the different brominating agents strongly suggest a common radical chain carrier. In fact, treating all of the data as applying to a single reaction yields  $\rho = -1.27$  with  $r = 0.945$ ,  $s = 0.15$ . A similar comparison has recently been carried out for several substituted N-bromosuccinimides by Martin,<sup>7</sup> and, since NBS and  $\text{Br}_2$  also show parallel reactivities,<sup>5,7,8</sup> he concludes that a bromine atom chain is involved in all his systems. The good fit of all of our data (including that on NBS) to a single  $\rho$ -value points to a similar conclusion here, further supported by the results described in the next section.

**Other Hydrocarbons.**—Relative reactivities of some other hydrocarbons are listed in Table II. The most critical reactivity is that of ethylbenzene, and values are again seen to be very close in all systems. Data for saturated hydrocarbons are subject to considerable uncertainty and may represent merely orders of magnitude. In any case, the results again support the hypothesis of a common bromine atom chain as the major reaction path, and suggest that as far as selectivity is concerned, all of the N-haloamides are equivalent for synthetic purposes.

**N-Chlorosuccinimide.**—The participation of chlorine atom chains in chlorinations involving N-chlorosuccinimide was first proposed by Goldfinger<sup>9</sup> and has been supported by deuterium isotope effect measurements by

(1) Taken from the Ph.D. Dissertation of Anne L. Rieger, Columbia University, 1962. Support of this work by a grant from the National Science Foundation is gratefully acknowledged.

(2) Socony Mobil Oil Co. Fellow 1960–1961.

(3) O. O. Orazi and J. Meseri, *Anales asoc. quim. argentina*, **37**, 142 (1949), and subsequent papers.

(4) A. Wohl, *Ber.*, **52B**, 51 (1919).

(5) C. Walling, A. L. Rieger, and D. D. Tanner, *J. Am. Chem. Soc.*, **85**, 3129 (1963).

(6) H. C. Brown and Y. Okamoto, *ibid.*, **80**, 4979 (1958).

(7) R. E. Pearson and J. C. Martin, *ibid.*, **85**, 354 (1963).

(8) G. A. Russell, C. De Boer, and K. M. Desmond, *ibid.*, **85**, 365 (1963).

(9) J. Adam, P. A. Gosselain, and P. Goldfinger, *Nature*, **171**, 704 (1953).