This product was also found in the thermal decomposition of **1a** in THF and in the photolysis of **11**.

Products from the Photolysis of 11 in THF. A 0.026 *M* solution of **11** in THF was degassed and irradiated at wavelengths ≥480 nm.

1-Oxa-8,10-di-*tert*-butylspiro[5.5]undeca-7,10-dien-9-one (14). This product and those already described were isolated by elution chromatography on Florisil: mp 51–54°; ir (film) 1665 and 1650 (carbonyl doublet); nmr $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}}$ 6.63 (s, 2.12, vinyl H), 3.71 (t, 2.00, CH_2), 1.61 (m, 6.72, CH_2), 1.20 (s, –, *t*-Bu); *m/e* 276 (molecular). Compound **14** is recovered unchanged after heating in CH_3OH with 10% HCl.

Photolysis of 1a in C_6H_6. A degassed 0.01 *M* benzene solution of **1a** was irradiated in Pyrex at a temperature of about 45° with RPR-3500 Å uv lamps for 5 days. After complete photolysis of **1a**, the decomposition products were worked up by extraction by $NaHCO_3$ and by glc (10% Carbowax on 20M TPA). No 2,6-di-*tert*-butyl-4-phenylphenol (**5**) was present. The yield of acid **4** was 0.41 mol/mol.

Acknowledgments. The authors wish to acknowledge support of this work by the National Science Foundation Grant GP 15991 and in part by U. S. Public Health Service Grant No. AM 10498 from the National Institute of Arthritis and Metabolic Diseases.

Polar Radicals. VI. Bromination Reactions with Molecular Bromine and *N*-Bromosuccinimide. Apparent Anomalies and Similarities[1]

Dennis D. Tanner,* Jeffrey E. Rowe,[2a] Tony Paće, and Yoshio Kosugi[2b]

Contribution from the Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada. *Received October 11, 1972*

Abstract: The relative rates of bromination of a number of alkanes and substituted alkanes have been determined. A comparison of the relative rates of bromination with high concentrations of *N*-bromosuccinimide (NBS) and with molecular bromine shows significant differences. These differences can be attributed, in part, to the polar effects on the transfer reactions between the substituted and unsubstituted alkyl radicals with hydrogen bromide. The differences observed between the two reagents are found to disappear when the brominations with molecular bromine are carried out at very high bromine concentrations where the transfer reaction with hydrogen bromide cannot compete effectively with the transfer reaction with molecular bromine. This observation further substantiates, at least at high concentrations of NBS in acetonitrile, the mechanism which has been proposed for NBS bromination reactions. The relative rates observed demonstrate the retarding effect of a neighboring bromine or chlorine atom on the hydrogen abstraction reactions of a bromine atom.

Free radical hydrogen abstraction reactions on electronegatively substituted alkanes by intermediates other than hydrogen atoms or carbon-centered radicals (eq 1) would be predicted to proceed at a slower rate than those of similar reactions carried out on the unsubstituted parent alkanes.[3,4] Polar repulsion between the incipient polar molecule YH and the new polar

$$Y\cdot + RH \longrightarrow [\cdot Y\ H\text{–}R \longleftrightarrow Y\text{–}H\ R\cdot]^{\ddagger} \longrightarrow YH + R\cdot \quad (1)$$

radical R· would be reflected by an increase in the energy requirements of the transition state and thereby a decrease in the rate of this reaction compared to the rate of the reaction of the unsubstituted alkane, where the new radical formed is not polar.

This precept could possibly be challenged if one considers the abstraction reactions on selected brominated and chlorinated alkanes, where neighboring group participation by the halogen atom has been proposed as being responsible for increased rates of reaction of the hydrogen atoms located on carbon atoms β to the halogen.[5,6] If the assistance were large enough to overcome the normal polar effects, the resulting rates of abstraction found for the substituted alkanes could be predicted to be faster than those of the parent hydrocarbon.

Some evidence can be found in the literature to rationalize the concept that bromination of halogenated alkanes proceeds at a rate faster than that of the parent alkane or of a less highly halogenated derivative.

Recently, Skell has reported results obtained from the competitive bromination of a number of halogenated alkanes *vs.* their unsubstituted analogs.[7] In all cases that he has reported, although the experimental conditions were not given, the brominated alkanes apparently reacted at a faster rate than their parent hydrocarbons. It is of interest to note that although *cis*- and *trans*-4-bromo-*tert*-butylcyclohexane should show a very similar polar effect, the relative rate of bromination has been reported to be $k_{\mathrm{cis}}/k_{\mathrm{trans}} > 15$.[8] In his more recent publication the cis isomer was reported to undergo bromination 19.2 times faster than cyclo-

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(1) Part V: D. D. Tanner, M. W. Mosher, N. C. Das, and E. V. Blackburn, *J. Amer. Chem. Soc.*, **93**, 5846 (1971).

(2) (a) Killam Memorial Predoctoral Fellow, 1969–1972; (b) University of Alberta Postdoctoral Fellow, 1970–1972.

(3) C. Walling, "Free Radicals in Solution," Wiley, New York, N. Y., 1957, p 361 *et seq.*

(4) J. M. Tedder, *Quart. Rev., Chem. Soc.*, **14**, 336 (1960).

(5) Assisted abstraction by neighboring chlorine has been proposed by Traynham and Skell; see J. G. Traynham and W. G. Hine, *J. Amer. Chem. Soc.*, **90**, 5208 (1968); H. Schweinsberg and J. G. Traynham, Abstracts, 158th National Meeting of the American Chemical Society, New York, N. Y., Sept 1969, No. ORGN 122; P. S. Skell, *Chem. Soc., Spec. Publ.*, **No. 19**, 137 (1964).

(6) For a review of the proposed evidence for participation by neighboring bromine during free radical abstraction, see W. A. Thaler, *Methods Free-Radical Chem.*, **2**, 166 (1969); L. Kaplan, "Bridged Free Radicals," Marcel Dekker, New York, N. Y., 1972.

(7) P. S. Skell and K. J. Shea, *J. Amer. Chem. Soc.*, **94**, 6550 (1972).

(8) P. S. Skell and P. D. Readio, *J. Amer. Chem. Soc.*, **86**, 3334 (1964).

hexane, a model for its parent hydrocarbon. The faster rate of bromination of the cis isomer was presumably (since the major product is reported to be the 1,2-dibromide) a result of abstraction of the β-axial hydrogen atom with concomitant assistance by the axial coplanar bromine. In the trans isomer, no such assistance is possible and, in fact, a large number of products are formed upon its bromination. However, from Skell's data the reaction of the trans isomer, if cyclohexane is a good model, will also be faster than, or as fast as, the unsubstituted alkane. Not too much credence can be placed on the stereochemical argument, however, since it has been shown by Cristol[9] that the rate of bromination of 5a-bromojanusene (RBr) was faster than that of the unsubstituted (RH) material ($k_{\mathrm{RBr}}/k_{\mathrm{RH}} = 2.8$ at 72° and 5.2 at 12°). In 5a-bromojanusene, the bromine atom and its β hydrogen are in a cis, coplanar geometry, and backside participation by the halogen atom is not possible during the abstraction of this hydrogen.

More direct evidence for the increased rate of bromination of substituted alkanes is the observation that a much greater than statistical amount of polyhalogenation has been observed in the vapor-phase bromination of 1-bromo- and 2-bromobutane.[10]

In order to test the hypothesis of neighboring group participation, the relative rates of bromination of a number of alkanes and halogenated alkanes have been determined using NBS or molecular bromine as the brominating agent. The systems used to study the effects of substitution on the rates of bromination are the ones claimed to show the largest effects from neighboring group participation by a β-bromine atom,[11] *viz.*, cyclohexyl,[12] 1-butyl,[12] 2-methyl-1-butyl,[13] and *cis*- and *trans*-4-*tert*-butylcyclohexyl[7,8] bromides.

Results and Discussion

In a radical-chain bromination where two substrates compete

$$\mathrm{Br}\cdot + \mathrm{R_1H} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{R_1}\cdot + \mathrm{HBr} \xrightarrow[k_3]{\mathrm{Br_2}} \mathrm{R_1Br} + \mathrm{Br}\cdot \qquad (2)$$

$$\mathrm{Br}\cdot + \mathrm{R_2H} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \mathrm{R_2}\cdot + \mathrm{HBr} \xrightarrow[k_4]{\mathrm{Br_2}} \mathrm{R_2Br} + \mathrm{Br}\cdot \qquad (3)$$

The ratio of rate constants can be computed from the relation

$$\log([\mathrm{R_1H}]_0/[\mathrm{R_1H}])/\log([\mathrm{R_2H}]_0/[\mathrm{R_2H}]) = k_1/k_2 \qquad (4)$$

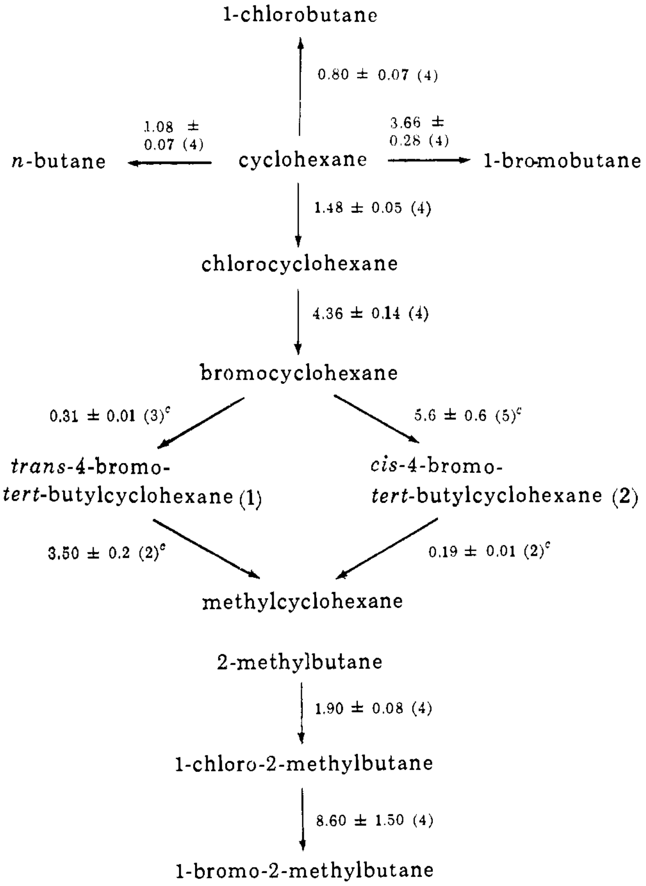
only if the abstraction reactions are irreversible processes. If appreciable reversal of the abstraction reaction occurs, the expression given by eq 5 must be used

$$\frac{d\ln(\mathrm{R_1H})}{d\ln(\mathrm{R_2H})} = \frac{k_1}{k_2}\left[\frac{1 + k_{-2}[\mathrm{HBr}]/k_4[\mathrm{Br_2}]}{1 + k_{-1}[\mathrm{HBr}]/k_3[\mathrm{Br_2}]}\right] \qquad (5)$$

to evaluate the relative rates of abstraction k_1/k_2. The integration and evaluation of (5) represents a more formidable challenge, and only in limiting cases can it be readily evaluated. Experimentally the reversal reaction can be made noncompetitive using either of two methods: the first method is to limit the amount of hydrogen bromide present in the system by carrying out the brominations using a large excess of NBS as a source of a low steady state concentration of molecular bromine; the second method is to carry out the brominations with such a large excess of molecular bromine that virtually all of the alkyl radicals produced are captured by transfer with molecular bromine.[14]

The rates of bromination of cyclohexane relative to its monobromo and chloro derivatives; butane relative to its 1-bromo and chloro derivatives and *cis*- and *trans*-4-bromo-*tert*-butylcyclohexane relative to each other and to cyclohexane, were determined by competitive bromination using 1:1:1 molar concentrations of the two substrates to that of molecular bromine ($\mathrm{R_1H}:\mathrm{R_2H}:\mathrm{Br_2}$). Relative rates of bromination were related to each other by the method schematically depicted on Chart I. The rate of bromination of 2-methylbutane was related to the bromination rates of its 1-bromo and chloro derivatives in a like manner and the results are also depicted in Chart I.

Chart I. Bromination with Molecular Bromine,[a,b] 40.0° ($\mathrm{R_1H}:\mathrm{R_2H}:\mathrm{Br_2} \simeq 1:1:1$)



[a] Arrows indicate direct competitions; numbers are relative reactivities per molecule at head of arrow to that at tail. The errors indicated are average deviations from the mean. [b] Number of experiments are in parentheses. [c] Run in $\mathrm{CCl_4}$ as solvent. All other experiments were run in "Freon 112."

The relative rates of bromination of these substrates

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[9] S. J. Cristol, M. A. Imhoff, and D. C. Lewis, *J. Org. Chem.*, **35**, 1722 (1970).

[10] M. S. Kharasch, W. S. Zinnt, and W. Nudenberg, *J. Org. Chem.*, **20**, 1430 (1955).

[11] Evidence against neighboring group participation in the free-radical bromination of these systems is presented in ref 1 and in D. D. Tanner, D. Darwish, M. W. Mosher, and N. J. Bunce, *J. Amer. Chem. Soc.*, **91**, 7398 (1969); D. D. Tanner, H. Yabuuchi, and E. V. Blackburn, *ibid.*, **93**, 4802 (1971).

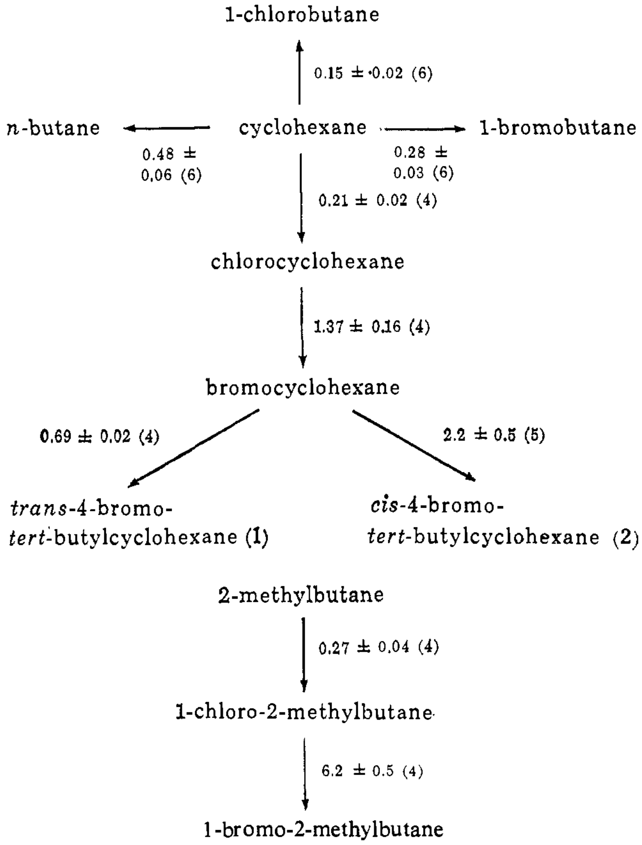
[12] W. Thaler, *J. Amer. Chem. Soc.*, **85**, 2607 (1963).

[13] P. S. Skell, D. L. Tuleen, and P. D. Readio, *J. Amer. Chem. Soc.*, **85**, 2849, 2850 (1963).

[14] R. E. Pearson and J. C. Martin, *J. Amer. Chem. Soc.*, **85**, 3142 (1963).

by NBS were related by the method schematically represented in Chart II.

Chart II. Bromination with NBS/AIBN,[a-c] at 40.0°
(R_1H:R_2H:NBS ≃ 1:1:8)



[a] All reactions were run in homogeneous acetonitrile solution, using AIBN as initiator. [b] Arrows indicate direct competitions; numbers are relative reactivities per molecule at head of arrow to that at tail. The errors indicated are average deviations from the mean. [c] Number of experiments is given in parentheses.

A comparison of the relative rates obtained by these two bromination methods is shown in Table I for the four systems that were studied.

Photobromination of Mixtures of Substrates with Molecular Bromine (R_1H:R_2H:Br_2 of 1:1:1). A superficial examination of the results obtained from the competitive brominations of the halogenated alkanes (Table I) indicates that with the exception of 1-chlorobutane all of the halogenated alkanes react at faster rates than their unsubstituted parent hydrocarbons. The values listed in Table I, however, are determined from the expression, eq 4, which assumes an irreversible abstraction process. The relative reactivities calculated using this expression are only apparent relative rates if there is significant reversal, and do not necessarily reflect the true kinetic values.

Table I. A Comparison of the Relative Rates of Bromination

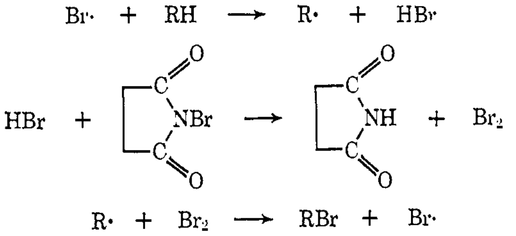
Condition	Relative rate H	Cl	Br	1[a]	2[b]
A. Of Cyclohexane and Substituted Cyclohexanes with NBS and Molecular Bromine at 40°					
$Br_2/h\nu$	1.00	1.48	6.45	2.00	36.1
NBS/$CH_3CN/h\nu^c$	1.00	0.23	0.41	0.21	0.86
NBS/CH_3CN/AIBN	1.00	0.21	0.29	0.20	0.63
B. Of 2-Methylbutane and 1-Substituted 2-Methylbutanes with NBS and Molecular Bromine at 40°					
	H	Cl	Br		
$Br_2/h\nu$	1.0	1.9	16.3		
NBS/$CH_3CN/h\nu^c$	1.0	0.29	1.61		
NBS/CH_3CN/AIBN	1.0	0.27	1.67		
C. Of Butane and 1-Substituted Butanes with NBS and Molecular Bromine at 40°					
	H	Cl	Br		
$Br_2/h\nu$	1.0	0.74	3.4		
NBS/CH_3CN/AIBN	1.0	0.31	0.58		

[a] *trans*-4-Bromo-*tert*-butylcyclohexane. [b] *cis*-4-Bromo-*tert*-butylcyclohexane. [c] Values were calculated using the same method as is given in Chart II.

It can be also seen that both *cis*- and *trans*-4-bromo-*tert*-butylcyclohexanes (**2** and **1**) are brominated at a faster "apparent" rate than cyclohexane, and that **1** is apparently 18 times less reactive than **2**.

Brominations of Alkanes and Substituted Alkanes with NBS. The mechanism for the NBS bromination of alkanes (Scheme I), which is generally accepted as proceeding by a bromine atom chain, has been established independently, for the substitution reactions of arenes and alkenes, by three groups of workers.[14-16] The reactivity of the NBS reagent and that of molecular bromine (in the absence of reversal) was found to be the same for the abstraction reactions of benzylic hydrogens. It is not inconceivable, however, that the mechanism is not the same for the energetically less favorable brominations of the substituted alkanes and this suggestion has recently been communicated.[17] We have recently established that the product distributions found for the brominations of bromocyclohexane and 1-bromobutane differ when the free-radical brominations are carried out in homogeneous acetonitrile solution with large excesses of NBS or with molecular bromine.[1] The two reactions presumably are both proceeding through a bromine atom chain, one (NBS) having limited reversal and one (Br_2) with hydrogen bromide reversal. An apparent increased rate of abstraction of the hydrogen β to the bromine atom, anchimeric assistance, is not a consistent rationalization to explain the almost exclusive production of 1,2-dibromides in the two systems when molecular bromine is used, since to be consistent product distribution in the NBS brominations, subject to the same effects, should be the same. As the β-hydrogen atoms in both substrates are not the most reactive hydrogen atoms in the NBS brominations, it was further necessary to test the NBS mechanism in the halogenation of substituted alkanes.

Scheme I



Although we have previously obtained material balances in the NBS brominations of 1-bromobutane

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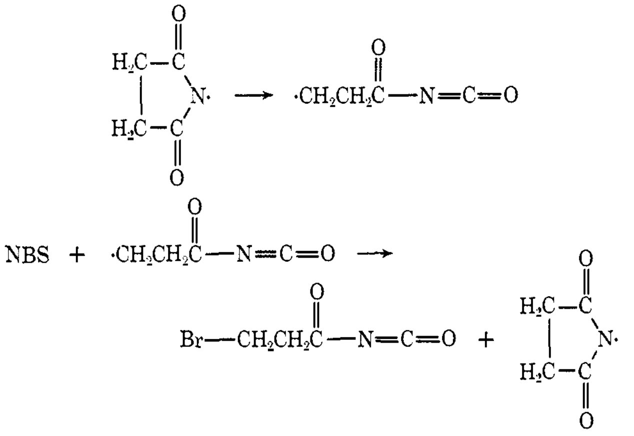
(15) C. Walling, A. L. Rieger, and D. D. Tanner, *J. Amer. Chem. Soc.*, **85**, 3129 (1963).

(16) G. A. Russell and K. M. Desmond, *J. Amer. Chem. Soc.*, **85**, 3139 (1963).

(17) J. G. Traynham, E. E. Green, Y. Lee, F. Schweinsberg, and C. Low, *J. Amer. Chem. Soc.*, **94**, 6552 (1972).

in acetonitrile,[18] the relative rates of bromination of a number of the substituted alkanes generally showed poor material balances; *i.e.*, the amount of active bromine that was consumed during the reaction could not be accounted for by analysis of the substrate bromination products.[19] The active bromine presumably could have been taken up by an acid-catalyzed bromination of the solvent, since we have demonstrated that small amounts of hydrogen bromide can catalyze the reaction of bromine with acetonitrile.[20] However, no bromoacetonitrile could be detected by glpc analysis of the reaction mixtures.

An alternative route for the disappearance of NBS, exclusive of the bromination of the solvent or the substrates, is the well recognized β-scission reaction for the chain decomposition of the reagent.[21]



Under the reaction conditions in which the competitive brominations were carried out, large amounts of β-bromopropinyl isocyanate could be detected by ir spectroscopy. Any isocyanate products could be quantitatively removed by the treatment with aqueous thiosulfate prior to the analysis. The observation of this side reaction presented the possibility that the results of the competitive bromination reactions using NBS were influenced by radical intermediates other than the bromine atom.

The reactivity observed in the NBS reactions was shown not to be due to a carbon-centered radical (arising from β scission of a succinimidyl radical) by comparing the reagent's reactivity with that of several other brominating reagents, *viz.*, 1,3-dibromo-5,5-dimethylhydantoin, 1-bromo-3,5,5-trimethylhydantoin, tetramethyl-*N*-bromosuccinimide. A comparison of the reactivity of these four *N*-bromo reagents is listed in Table II. The results of these competitive brominations clearly indicate that within experimental error all of the *N*-bromo brominating agents show the same reactivity, *i.e.*, that of the bromine atom, unless fortuitously all of these structurally different reagents have nitrogen radicals which all show the same selectivity.

Table II. A Comparison of the Relative Rates of Bromination of a Number of Substrates Using Different Brominating Reagents and Conditions[a]

Substrate		Brominating reagents[b,c] and conditions	No. of reactions	k_{R_1H}/k_{R_2H}
R_1H	R_2H			
1-Bromobutane	Cyclohexane	A	2	0.58 ± 0.10
		B	2	0.62 ± 0.09
		C	2	0.66 ± 0.02
		D	2	0.52 ± 0.02
		G	2	0.32 ± 0.02
Chlorocyclohexane	Cyclohexane	A	6	0.23 ± 0.02
		B	2	0.14 ± 0.02
		C	3	0.43 ± 0.01
		D	4	0.36 ± 0.03
		E	2	0.18 ± 0.02
		G	3	0.29 ± 0.02
Bromocyclohexane	Chlorocyclohexane	A	6	1.80 ± 0.20
		B	3	1.58 ± 0.05
		C	3	1.87 ± 0.03
		E	2	1.88 ± 0.09
2	Bromocyclohexane	A	3	2.1 ± 0.3
		B	2	2.0 ± 0.3
		C	3	2.8 ± 0.1
		E	2	2.8 ± 0.3
		F	2	2.7 ± 0.2

[a] All reactions were photoinitiated. [b] A, NBS; B, tetramethyl-*N*-bromosuccinimide; C, 1,3-dibromo-5,5-dimethylhydantoin; D, bromine, molar ratio $R_1H:R_2H:Br_2$ of 1:1:100; E, 1-bromo-3,5,5-trimethylhydantoin; F, bromine, molar ratio $R_1H:R_2H:Br_2$ of 1:1:30; G, NBS:$R_1H:R_2H:Br_2$ of 8:1:1:0.4. [c] A, B, C, E, and G in solvent acetonitrile.

Conceivably a mixed chain, abstraction by succinimyl radicals and bromine atoms, can be proposed for the NBS brominations with unreactive substrates. The probability of the NBS reaction proceeding by a mixed chain would be rather low if an appreciable amount of molecular bromine were always present throughout the reaction. When the relative rates of bromination of cyclohexane to cyclohexyl chloride or 1-bromobutane to cyclohexane were determined using an acetonitrile mixture of the two substrates, molecular bromine and NBS (NBS:Br_2:R_1H:R_2H of 8:0.4:1:1), the same relative rates of reaction were obtained as were found in the NBS brominations (see Table II).

Competitive Brominations of Mixtures of Substrates with NBS (R_1H:R_2H:NBS of 1:1:8). In the present study, relative kinetics using NBS as the brominating agent were carried out in homogeneous acetonitrile solution, using either photochemical or AIBN initiation as described in an earlier paper.[1] The results listed in Table I show that in all cases the rates of bromination with NBS of the halogenated alkanes relative to the parent hydrocarbon are significantly slower than they are with molecular bromine. The competitive rates of bromination with NBS of the 1-substituted butanes and the monosubstituted cyclohexanes are all slower than the parent hydrocarbons as would be predicted from a consideration of the polar effects of the substituent on a hydrogen abstraction by a bromine atom. Only in the case of 1-bromo-2-methylbutane, where the rate is lowered by a factor of 10 by bromination with NBS rather than with molecular bromine, is the relative rate of bromination with NBS slightly larger (1.68) than for

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(18) D. D. Tanner, D. Darwish, M. W. Mosher, and N. J, Bunce, *J. Amer. Chem. Soc.*, **91**, 7398 (1969).

(19) Competitive brominations in methylene chloride, a solvent in which NBS has a minimal solubility (0.29 *M*),[13] likewise, showed an even poorer material balance. A substantial amount of the consumed active bromine (~30%) could be accounted for as bromodichloromethane, while only about 30% was accounted for as product. The values of the relative rates obtained in this solvent, as had been reported previously,[15] were found to be irreproducible.

(20) Unpublished results from this laboratory.

(21) (a) J. C. Martin and P. D. Bartlett, *J. Amer. Chem. Soc.*, **79**, 2533 (1957); (b) H. W. Johnson, Jr., and D. E. Bublitz, *ibid.*, **79**, 753 (1957); **80**, 3150 (1958).

the parent hydrocarbon.[22] It must be pointed out that in this case if neighboring group participation were operative, the assistance would be required to help the abstraction of a tertiary hydrogen, an energetically less useful process, while in the other systems assisted abstraction of a secondary hydrogen is not seen.

Competitive Brominations of Mixtures of Substrates with High Concentrations of Molecular Bromine. The alternative method of limiting the importance of the reversal of hydrogen bromide upon the competitive brominations was to run the reactions in the presence of high concentrations of molecular bromine. Competitive transfer reactions having similar rate constants, k_t and $k_{t'}$, can be affected by changing the concentration of the transfer agents so that either path can become dominant.

$$R\cdot + HBr \xrightarrow{k_t} RH + Br\cdot$$

$$R\cdot + Br_2 \xrightarrow{k_{t'}} RBr + Br\cdot$$

Several of the relative rate determinations that showed the greatest differences when determined by molecular bromine (1:1:1) bromination compared to NBS bromination were carried out using large excesses of molecular bromine. The reactants studied were shown to be stable to the high concentrations of bromine present in the reaction and their stabilities were also affirmed in the presence of bromine with added hydrogen bromide. The relative rates of these substrates determined in the presence of increasing amounts of molecular bromine changed from the values determined for low concentrations of bromine (1:1:1) to the values obtained in the NBS reactions (see Table III).

In the case of the relative reactions using 4-bromo-*tert*-butylcyclohexanes and bromocyclohexane, the value obtained with NBS could not be achieved by increasing the concentration of molecular bromine since it was found that at the concentrations of bromine necessary to reach this limit the substrates were not stable.

The observation, that the relative rates of bromination of the substrates using high concentrations of molecular bromine are the same as, or approximate, the values obtained with NBS, is strong support for the proposal that both reactions proceed *via* a mechanism which involves the same abstracting species.

Table III. A Comparison of the Relative Rates of Brominations Using NBS or Increasing Concentrations of Bromine at 40.0°

Substrates R_1H	R_2H	Molar ratio R_1H: $R_2H:Br_2$	No. of runs	k_{R_1H}/k_{R_2H}
1-Bromobutane	Cyclohexane	1:1:1	4	3.7 ± 0.3
		1:1:5	3	1.61 ± 0.12
		1:1:20	2	1.06 ± 0.04
		1:1:100	2	0.52 ± 0.01
		1:1:NBS[a]	2	0.58 ± 0.1
Chlorocyclohexane	Cyclohexane	1:1:1	4	1.48 ± 0.05
		1:1:6	3	1.02 ± 0.07
		1:1:20	2	0.68 ± 0.02
		1:1:40	2	0.56 ± 0.04
		1:1:100	3	0.36 ± 0.03
		1:1:NBS[b]	4	0.23 ± 0.02
Bromocyclohexane	Chlorocyclohexane	1:1:1	4	4.4 ± 0.1
		1:1:5	3	2.7 ± 0.02
		1:1:NBS[b]	4	1.8 ± 0.02
Bromocyclohexane	**1**	1:1:1	3	3.23 ± 0.01
		1:1:30	2	2.56 ± 0.02
		1:1:NBS[b]	3	1.92 ± 0.05
2	Bromocyclohexane	1:1:1	5	5.6 ± 0.6
		1:1:20	6	3.7 ± 0.4
		1:1:30	2	2.8 ± 0.2
		1:1:NBS[b]	4	2.1 ± 0.5

[a] Photoinitiated reactions of $R_1H:R_2H:NBS$ of 1:1:8 in acetonitrile. The reactions were carried out as were the reactions in Table I. [b] Values taken from the photoinitiated reactions in Table I.

Mechanistic Conclusions

A mechanistic scheme, which is consistent with the large body of information that exists on free radical bromination reactions, is available to explain, at least in part, these results. By the principle of microscopic reversibility, the readily reversible abstraction reactions of bromine atoms will be subject to the same polar effects in the reverse transfer reaction as are present in the forward hydrogen abstraction. If reversal is important, then a nonpolar carbon-centered radical will reverse "normally" (not subject to polar interactions) with hydrogen bromide and return to starting material in addition to transferring with bromine to form products; while a polar carbon-centered radical will be deactivated to reversal, but react in a manner unaffected by polar interactions with the nonpolar bromine molecule to give the bromination product. The net result of this sequence of reactions is an apparent increase in the rate of reaction of the polar molecule. The kinetic inequality, similar to that defined for the positional preference for substitution (1,2-bromination) in 1-bromobutane and bromocyclohexane can be expressed for the relative rates reported here.

$$(\text{rate}_{HBr}/\text{rate}_{Br_2})^{\text{nonpolar}} > (\text{rate}_{HBr}/\text{rate}_{Br_2})^{\text{polar}}$$

The differences between the brominations with low concentrations of bromine ($R_1H:R_2H:Br_2$ of 1:1:1) and those of high concentrations of NBS or the brominations with high ratios of bromine must be accounted for, at least in part, by a consideration of these effects.

Since the publication of our first paper,[18] which questioned the concept of anchimeric assistance by neighboring bromine during the hydrogen abstraction reactions of a bromine atom, we have attempted to obtain more quantitative data concerning the relative rates of transfer of the radicals produced during the bromination of 1-bromobutane. The dependence of the isomer distribution on the percentage reaction (*i.e.*, hydrogen bromide concentration) has been confirmed; however, we have been unable, as has been recently claimed[7,17] to repeat the observation that at 18% or less reaction the 1,3-dibromide was the major product. We have established, however, using deuterium labeled 1-bromobutane that the proposed relationship between the transfer rates at the γ and β positions, which was used to explain the dependence of the isomer distribution on the percentage reaction was, indeed, valid.[23]

$$(\text{rate}_{HBr}/\text{rate}_{Br_2})^{\gamma} > (\text{rate}_{HBr}/\text{rate}_{Br_2})^{\beta}$$

The possibility still exists that the apparent kinetic reactivity of the bromine atom in solution, even in the

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[22] Since the NBS brominations only approximate reactions carried out in the absence of hydrogen bromide,[1] small amounts of residual reversal can explain the small amount of enhancement.

[23] D. D. Tanner, Y. Kosugi, R. J. Arhart, and N. Wada, *J. Amer. Chem. Soc.*, submitted for publication.

absence of significant reversal with external hydrogen bromide, may be subject to reversal with hydrogen bromide formed within a solvent cage (see Scheme II),

Scheme II

$$\mathrm{RH} + \mathrm{Br}\cdot \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \underbrace{(\mathrm{R}\cdot + \mathrm{HBr})}_{\text{solvent cage}} \underset{k_{-d}}{\overset{k_d}{\rightleftarrows}} \mathrm{R}\cdot + \mathrm{HBr} \underset{\mathrm{Br_2}}{\overset{k_2}{\rightleftarrows}} \mathrm{RBr} + \mathrm{Br}\cdot$$

and that competitive with diffusion, k_d, the reversal reaction within the cage will be subject to the same kinetic influences as are seen with reversal with external hydrogen bromide.[23]

If, however, significant cage reversal with hydrogen bromide does occur in the brominations using molecular bromine, then this type of process is also possible in NBS brominations. This apparent anomaly suggests the possibility that the solvent, acetonitrile, may, by complexing with hydrogen bromide, slow down the reversal reaction.

Experimental Section

Materials. 1-Bromobutane and bromocyclohexane were purified in the manner described previously.[1] 1-Chlorobutane and chlorocyclohexane were similarly purified. Cyclohexane and *n*-butane were Phillips research grade chemicals and were used as supplied. Spectroquality 2-methylbutane (Matheson Coleman and Bell) was distilled before use.

1-Bromo-2-methylbutane, bp 117–119° (705 mm), $n^{20}\mathrm{D}$ 1.4455 (lit.[24] bp 121.6° (760 mm), $n^{20}\mathrm{D}$ 1.4451), was prepared by the method of Crombie and Harper.[25]

1-Chloro-2-methylbutane, bp 96.5° (695 mm), $n^{20}\mathrm{D}$ 1.4126 (lit.[26] bp 100.5° (760 mm), $n^{20}\mathrm{D}$ 1.4124), was prepared from the alcohol by treatment with thionyl chloride and pyridine.[26]

cis-4-Bromo-*tert*-butylcyclohexane was prepared from the commercial mixture of 4-*tert*-butylcyclohexanols and phosphorus pentabromide[27] or, more conveniently, by use of tri-*n*-octyl phosphine.[28] The crude monobromide obtained by distillation was recrystallized from pentane at −25 and at 0°, and finally distilled through a 20-in. spinning band column, yielding *cis*-4-bromo-*tert*-butylcyclohexane, bp 68° (1.9 mm), $n^{25}\mathrm{D}$ 1.4896 (lit.[27] bp 70° (2 mm), $n^{20}\mathrm{D}$ 1.4912). Analysis by glpc (10% DEGS on Chromosorb P DMCS AW, 18 ft × 0.25 in. glass column, 150°) indicated the sample contained 97% cis bromide, 2.3% trans bromide, and 0.7% of another impurity of very similar retention time. The infrared absorptions agreed with those reported.[27] The nmr spectrum ($\mathrm{CCl_4}$ solution, Varian A-60) was consistent with a cis configuration of the bromide, showing a characteristic equatorial proton absorption at δ 4.60 (275 cps *vs.* TMS, base width of 15 cps; *cf.* lit.[29] δ 4.62).

trans-4-Bromo-*tert*-butylcyclohexane was prepared by the selective dehydrobromination of the cis isomer,[27] from a mixture of the two bromides obtained by the Cristol–Firth[30] modification of the Hunsdiecker reaction on 4-*tert*-butylcyclohexanecarboxylic acid.[31] Distillation through a 20-in. spinning band column and recrystallization from pentane at −72° gave the pure trans isomer, bp 49° (0.5 mm), $n^{21.9}\mathrm{D}$ 1.4870 (lit.[25] bp 120° (24 mm), $n^{20.2}\mathrm{D}$ 1.4868). Glpc showed the sample to contain 98.5% of the trans isomer and 1.5% of the cis. The infrared spectrum agreed with that reported[27] and the nmr spectrum ($\mathrm{CCl_4}$ solution, Varian A-60) was consistent with the trans configuration of the bromide, showing the characteristic axial proton absorption at δ 3.83 (229 cps *vs.* TMS, base width 42 cps, lit.[29] δ 3.81).

N-Bromosuccinimide (NBS) was purified by rapid recrystallization from hot water and dried in a vacuum desiccator over phosphorus pentoxide; iodometric titration showed its purity to be always >98%.

1,3-Dibromo-5,5-dimethylhydantoin, 100% pure by titration, was obtained from Arapahoe Chemicals and used without further purification. 1-Bromo-3,5,5-trimethylhydantoin, 99.5% pure by titration, was prepared from 5,5-dimethylhydantoin,[32] utilizing the mild conditions developed by Brownlee[33] for the bromination of the hydantoin. Tetramethyl-*N*-bromosuccinimide, 100.5% pure by titration, was prepared from azobisisobutyronitrile.[15]

Bromine was washed with concentrated sulfuric acid and distilled from phosphorus pentoxide and/or molecular sieve Type 4A prior to use. Acetonitrile was purified by the method of O'Donnell,[34] dried by distillation from calcium hydride, and stored in a drybox prior to use.

Analysis. The butane, 2-methylbutane, and cyclohexane systems were analyzed on either a 10% DEGS on Diatoport 30 ft × 0.25 in. or on a 20% DIDP on Chromosorb W-AW, 12 ft × 0.25 in. using all glass columns. Several of the rates involving 1-bromobutane were checked using a 10% Carbowax 20M, 10 ft × 0.25 in. stainless steel column. *cis*- and *trans*-4-bromo-*tert*-butylcyclohexane were analyzed using either a 10% DEGS on Chromosorb P-AW DMCS, 18 ft × 0.25 in. or on a 20% DIDP on Chromosorb W-AW 6 ft × 0.25 in. all glass columns. All compounds studied were stable on the columns used. Peak areas were calculated by the peak height–peak width method or by means of a Disc or electronic integrator; the methods used were consistent with each other. Relative reactivities were calculated by the method reported previously by this laboratory.[35]

Competitive Bromination with Molecular Bromine ($\mathbf{R_1H:R_2H:Br_2}$ of 1:1:1). The reaction mixtures consisted of a 1:1:1 mole ratio of $\mathrm{R_1H:R_2H:Br_2}$ in Freon 112 or carbon tetrachloride as solvent. Freon 112 or *o*-dichlorobenzene were used as internal standards, both gave identical results within experimental error. The reaction mixtures were prepared by pipetting an aliquot of a solution containing the two substrates and the internal standard into a 4-ml tube containing a known amount of bromine. The resulting solution (1 ml) was degassed by the freeze–thaw method and sealed. The reaction tubes were irradiated at 40.0 ± 0.1° with 2 × 200-W incandescent lamps until all the bromine color disappeared.

Competition Bromination with Succinimides and Hydantoins. All reactions were carried out in homogeneous acetonitrile solutions. Reaction mixtures consisted of a 1:1:8 mole ratio of $\mathrm{R_1H:R_2H}$:brominating agent and an internal standard in sealed, degassed tubes. Thermal reactions contained a catalytic amount of AIBN (1 mol % based on the brominating agent) and were carried out at 40.0 ± 0.5° in the dark for an appropriate period of time (~800 hr). Photolytic experiments were conducted at 40.0 ± 0.1° by irradiation with either one 60-W or two 40-W incandescent lamps for a time sufficient to ensure at least 10% reaction for each component.

A typical reaction mixture contained 1.3×10^{-4} mol of each substrate and 1.0×10^{-3} mol of NBS (1.0×10^{-5} mol of AIBN for a thermal reaction) in 2.5 ml of acetonitrile. After reaction, the organic reactants and products were separated from the brominating agent either by vacuum distillation or by destruction of the brominating agent with aqueous potassium iodide acidified with mineral acid followed by extraction with pentane, Freon 113, or *o*-dichlorobenzene. Control experiments indicated that both procedures gave >98% recovery of substrates and internal standard. In either case the amount of brominating agent remaining was determined by titration with standard sodium thiosulfate solution. In a typical competition between *cis*-4-bromo-*tert*-butylcyclohexane and bromocyclohexane, after irradiation with two 40-W incandescent lamps for 3 hr, 24% (2.40×10^{-4} mol) of the NBS had been consumed; 46% (5.98×10^{-5} mol) of the cis, and 23% (2.99×10^{-5} mol) of the bromocyclohexane had reacted leading to a relative rate of 2.35.

Reactions run using a mixture of NBS and molecular bromine ($\mathrm{NBS:R_1H:R_2H:Br_2}$, 8:1:1:0.4) were run in the manner described for the photolytic reactions of NBS alone.

Competition Reaction with Excess Bromine. The reaction

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mixtures consisted of varying ratios of $R_1H:R_2H:Br_2$ from 1:1:5 to 1:1:100 with Freon 112 as the internal standard in sealed, degassed tubes. The tubes were irradiated at 40.0 ± 0.1° until at least 10% of each substrate had reacted. The excess bromine was destroyed with ice-cold aqueous sodium bisulfite. The organic substrates were extracted with a suitable solvent (Freon 113 or *o*-dichlorobenzene), washed once with cold water, and dried over anhydrous sodium sulfate.

The stability of the substrates in excess bromine in the dark was checked both with and without added hydrogen bromide. Bromocyclohexane and *cis*-4-bromo-*tert*-butylcyclohexane were found to be unstable in a 100-fold mole excess of bromine but over at least 10 half-lives they were stable in a 30-fold mole excess of bromine, with equivalent amounts of added hydrogen bromide. The other substrates were stable to equivalent amounts of hydrogen bromide and 100-fold excess of molecular bromine.

Acknowledgment. The authors wish to thank the National Research Council of Canada and the University of Alberta for their generous support of this work.

Ionization of Nitrogen and Oxygen Acids in Strongly Basic Systems

A. Albagli, A. Buckley, A. M. Last, and Ross Stewart*

Contribution from the Department of Chemistry,
University of British Columbia, Vancouver 8, British Columbia, Canada.
Received August 21, 1972

Abstract: The ionization of three types of weak acid (neutral nitrogen and oxygen acids and anionic nitrogen acids) has been compared in aqueous and methanolic dimethyl sulfoxide (DMSO) solutions. The H_- scales for the nitrogen acids (aromatic amines) and the oxygen acids (any of several hindered phenols) diverge as the DMSO concentration increases, with the medium's basicity being much greater toward the nitrogen acids. The pK values of the latter tend to be larger in methanolic than in aqueous DMSO. A unique scale for phenols cannot be constructed over the whole range of solvent compositions because the compound's ionization curves are not all parallel. Indeed, addition of DMSO to aqueous hydroxide, up to about 20 mol %, *reduces* the basicity of the system toward hindered phenols. This does not occur when DMSO is added to methanolic methoxide, nor with nitrogen acids in either medium.

In the last decade, there has been considerable interest in strongly basic systems, and a number of groups have used the general Hammett technique to construct acidity scales in the region beyond pH 14.[1] In some cases bases have simply been added in larger and larger amounts to water, methanol, or like solvent. In others a fixed amount of base (*e.g.*, 0.01 M $(CH_3)_4N^+OH^-$) is used and a polar aprotic solvent such as dimethyl sulfoxide (DMSO) is added in larger and larger amounts. The H₋ function, which is defined as

$$H_- = pK_{HA} - \log [HA]/[A^-] = -\log \frac{a_{H^+} f_{A^-}}{f_{HA}}$$

governs the ionization of a neutral acid ($HA \rightleftharpoons H^+ + A^-$) and its generality depends on the activity coefficient ratio f_{A^-}/f_{HA} being dependent only on the composition of the medium and not on the identity of the various indicators used to construct the scale.

Other papers in this series[1e,f] have shown that the H_- function for a 0.01 M solution of tetramethylammonium hydroxide changes from 12 in water (H_- = pH in pure water) to 26 in 99.6 mol % DMSO. The organic acids used to construct this scale were a series of anilines and diphenylamines, and a number of tests have been applied to demonstrate the general validity of the pK and H_- values thus obtained. Carbon acids are less well behaved, however, and numerous cases are known of relative pK values being transposed when the medium is changed.[1d] We shall see from the subsequent discussion that oxygen acids, too, behave rather badly in this regard.

Anionic nitrogen acids generate a somewhat different scale,[1h] designated H_{2-}, because the activity coefficient ratio is affected by the charge type of the acid and conjugate base.

The present work was undertaken to determine the degree of divergence of acidity function behavior caused by variations in structure and charge in the indicators. The latter were either neutral nitrogen acids, monoanionic nitrogen acids, or neutral oxygen acids.

The nitrogen acids were all diphenylamines. The only oxygen acids sufficiently weak to be but partially ionized in strongly basic media are alcohols and certain hindered phenols. The former do not undergo a measurable spectral shift on ionization and hence are unsuitable for this study. Bulky ortho groups cause a considerable reduction in the acidity of phenols, presumably because of steric hindrance to the solvation of the phenoxide ion.[2]

Experimental Section

Those diphenylamines not previously prepared[1e,f,h] are described below. Their pK_{HA} values refer to water as the standard state; the

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