otherwise indicated), and sealed with a Teflon needle valve. The photolyses were effected without stirring at ambient temperature. The reaction course was followed by withdrawing the cuvette at convenient time intervals and examining spectrophotometrically after thorough agitation. The final concentration of *N*-halo imide was determined by iodometric titration.

Photolysis of *N*-Bromosuccinimide in CH_2Cl_2 in the Presence of 3,3-Dimethyl-1-butene at 313 nm. NBS (5.6×10^{-1} mmol), CH_2Cl_2 (54.6 mmol), and 3,3-dimethyl-1-butene (1.6×10^{-1} mmol) were irradiated for 1.5 h. (a) UV absorbances at λ_{313} (time, min): 1.52 (0), 1.47 (5), 1.27 (10), 1.07 (15), 0.96 (20), 0.79 (30), 0.64 (40), 0.39 (75), 0.32 (90). At 90 min, 18% of NBS remained. $\Phi = 66.7$ mol einstein^{-1}. (b) nondegassed UV absorbances at λ_{313} (time, min): 1.52 (0), 1.52 (5), 1.52 (15), 1.43 (30), 1.24 (45), 1.14 (60), 0.95 (90). At 90 min, 57% of NBS remained. $\Phi = 17.0$ mol einstein^{-1}. (c) in the presence of 2,6-di-*tert*-butyl-*p*-cresol (1.0×10^{-2} mmol), 96% of NBS remained after 90 min (no brominated products).

Photolysis of *N*-Bromosuccinimide in CH_2Cl_2 in the Presence of 3,3-Dimethyl-1-butene and 2,2′-Azobis(isobutyronitrile) at 366 nm. NBS (5.6×10^{-1} mmol), CH_2Cl_2 (54.6 mmol), 3,3-dimethyl-1-butene (1.6×10^{-1} mmol), and AIBN (2.0×10^{-1} mmol) were irradiated for 7.0 h; UV absorbances at λ_{366} (time, min) 0.71 (0), 0.67 (420). At 420 min, 41% of NBS remained with 6% dissociated AIBN. The work of Hammond[16] on the thermal decomposition of AIBN led to a value of 0.46 for the fraction of the total number of AIBN decompositions that yield kinetically "free" radicals. By utilization of this value, in conjunction with the amount of dissociated AIBN and consumed NBS, a chain length of 30 was obtained.

Photolysis of *N*-Bromosuccinimide in CH_2Cl_2 in the Presence of Neopentane and Bromine. NBS (5.6×10^{-1} mmol), CH_2Cl_2 (54.6 mmol), *neo*-C_5H_{12} (2.0 mmol), and Br_2 (6.65×10^{-3} mmol) were irradiated for 2.0 h; (a) At 313 nm, UV absorbances at λ_{313} (time, min): 1.54 (0), 1.53 (5), 1.49 (25), 1.42 (50), 1.25 (95), 1.14 (120). At 120 min, 69% of NBS remained with 0% consumed Br_2. $\Phi = 8.1$ mol einstein^{-1}. (b) At 366 nm, $\Phi = 9.0$ mol einstein^{-1}.

Acknowledgment. Financial support for this work came from the National Science Foundation (Grant CHE-7810049).

Registry No. 1, 72323-45-6; **2**, 66633-57-6; **3**, 82621-75-8; NBS, 128-08-5; NIS, 516-12-1; 2,2-Me_2-NCS, 82621-76-9; 2,2-Me_2-NBS, 82621-77-0; 2,3-Me_2-NBS, 82621-78-1; 2-Me-NBG, 82621-79-2; 2,2-Me_2-NBG, 82621-80-5; NCS, 128-09-6; 2,3-Me_2-NCS, 82621-81-6; NCG, 82621-82-7; NBG, 3699-18-1; 3,3-Me_2-NCG, 82621-83-8; 3,3-Me_2-NBG, 66393-63-3; neopentane, 463-82-1; 3,3-dimethyl-1-butene, 558-37-2; 2,2-dimethylsuccinimide, 3437-29-4; 2,2-dimethylglutarimide, 1194-33-8; 2-methylglutarimide, 29553-51-3; *dl*-2,3-dideuteriosuccinic acid, 21156-52-5; *dl*-2,3-dideuteriosuccinic anhydride, 80655-73-8; methyl *dl*-2,3-dideuteriosuccinamate, 82621-84-9; *meso*-2,3-dideuterio-*N*-bromosuccinimide, 66996-78-9; *meso*-2,3-dideuterio-*N*-chlorosuccinimide, 66996-79-0; *dl*-2,3-dideuterio-*N*-bromosuccinimide, 82621-85-0; β-bromopropionyl isocyanate, 18926-24-4; 1,1-dichloroethylene, 75-35-4; ethylene, 74-85-1; allene, 463-49-0; *N*-(2-chloro-1-ethyl)succinimide, 41212-96-8; 3-iodopropanoyl isocyanate, 82621-86-1; 3-bromo-3-methylbutanoyl isocyanate, 82621-87-2; 3-chloro-3-methylbutanoyl isocyanate, 82621-88-3; methyl *N*-(3-chloro-3-methylbutanoyl)carbamate, 82621-89-4; 3-bromo-2-methylbutanoyl isocyanate, 82621-90-7; methyl *N*-(3-bromo-2-methylbutanoyl)carbamate, 82621-91-8; 4-bromo-4-methylpentanoyl isocyanate, 82621-92-9; methyl *N*-(4-bromo-4-methylpentanoyl)carbamate, 82621-93-0; *N*-(2-bromo-3,3-dimethyl-1-butyl)-2-methylglutarimide, 82621-94-1; 4-bromopentanoyl isocyanate, 82621-95-2; methyl *N*-(4-bromopentanoyl)carbamate, 82621-96-3; neopentyl bromide, 630-17-1; neopentyl iodide, 15501-33-4; neopentyl chloride, 753-89-9; 2,3-dideuterio-β-bromopropionyl isocyanate, 82621-97-4; methyl *N*-(2,3-dideuterio-β-bromopropionyl)carbamate, 82638-76-4.

Reactions of a Graded Set of Radicals with *N*-Bromosuccinimide; Two Transition States

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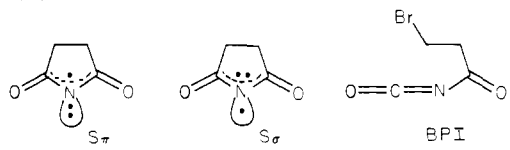
Contribution from the Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802. *Received November 9, 1981*

Abstract: The reactions of *N*-bromosuccinimide with a series of radicals have been studied. These reactions fall into two categories, the more reactive radicals producing σ-succinimidyl and the less reactive radicals producing π-succinimidyl. The threshold for the changeover from one reaction domain to the other occurs with radicals less reactive than secondary alkyls. These results are interpreted with two transition states, an in-line transition state for the more reactive radicals and an out-of-plane transition state for the less reactive radicals. An upper limit of 18 kcal/mol is established for the enthalpy difference, $H_{S_\sigma} - H_{S_\pi}$. Two new methods for generating S_π radicals are indicated.

Radical chain reactions in systems containing *N*-bromosuccinimide can be carried out (1) in the presence of Br_2 or (2) in the absence of Br_2 by including small amounts of appropriate bromine-scavenging alkenes.[1,2] With low-reactivity substrates (neopentane, *tert*-butyl chloride, methylene chloride), the substitution of Br for H must be attributed to a hydrogen abstractor that is far more reactive than Br· or R·, thus making succinimidyl(s) (**1** and **2**) the chain carrier(s). The two sets of reaction



1 2 3

conditions described above involve intermediates with distinctly different selectivities in H abstractions for these low-reactivity substrates. Also, in the presence of Br_2, there is no accompanying ring-opening reaction producing β-bromopropionyl isocyanate (BPI, **3**), whereas in the presence of bromine-scavenging alkenes, BPI is the major product.[1-3] These two lines of evidence led to the conclusion that the thermal chain reactions involving succinimidyl radicals operated with either the π or the σ states of the radical, depending only on which reaction (reaction 2 or 3) produced the succinimidyl.[1,2]

with Br_2 present

$$1^\circ\ R\cdot + Br_2 \rightarrow RBr + Br\cdot \quad (1)$$

$$Br\cdot + NBS \rightarrow Br_2 + S_\pi \quad (2)$$

with Br_2 scavenged

$$1^\circ\ R\cdot + NBS \rightarrow RBr + S_\sigma \quad (3)$$

(1) Skell, P. S.; Day, J. C. *Acc. Chem. Res.* **1978**, *11*, 381–387.
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(3) Tlumak, R. T.; Day, J. C.; Slanga, J. P.; Skell, P. S. *J. Am. Chem. Soc.*, preceding paper.

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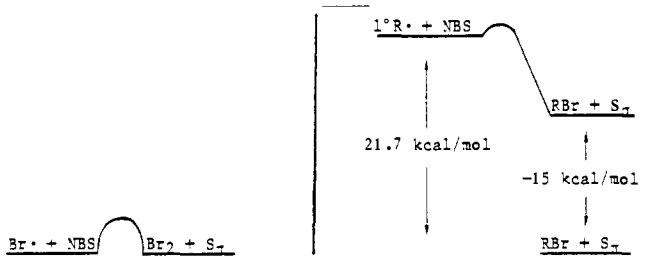


Figure 1.

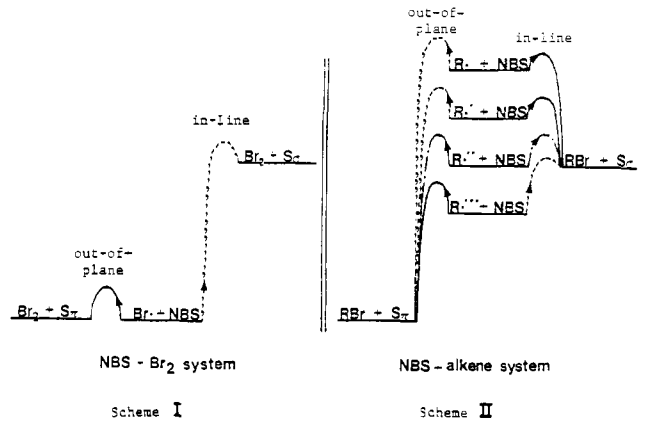
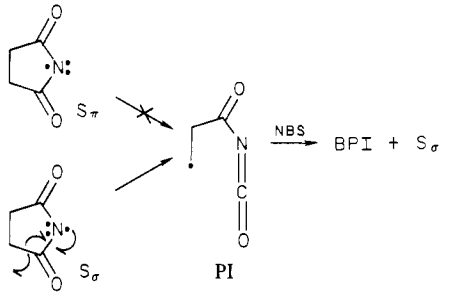


Figure 2.

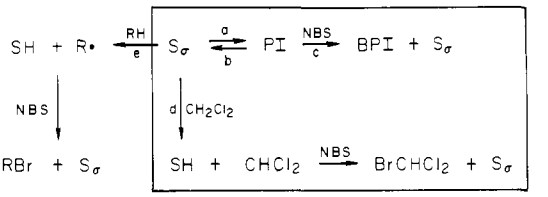
The reaction of Br· with NBS produces S_π (no ring opening), whereas the reaction of 1° R· with NBS produces S_σ (substantial ring opening). These reaction systems are remarkably clean, there being no indication of cross-contamination.



S_π or S_σ + 1° RH → 1° R· + SH (succinimide)

If the best estimate of the N–Br bond strength of NBS[4] is accepted at face value, reaction 2 is thermoneutral. Regardless of the accuracy of this value, reaction 3 would be 21.7 kcal/mol more exothermic if the identical succinimidyl radical (S_π) was produced (this value is the difference in dissociation energy for 1° R–Br and Br–Br). To avoid endothermic steps in the chain sequences the energy difference between S_σ and S_π was arbitrarily chosen as ~15 kcal/mol[5] (Figure 1; the energy diagram drawing is normalized by placing Br_2 and R–Br at the same level).

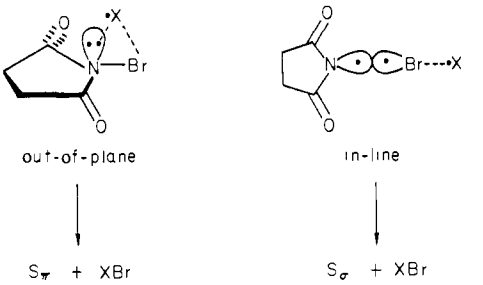
Scheme III



The striking feature of this system is that the reaction of 1° R· with NBS follows the less exothermic pathway to S_σ. While this behavior is not unprecedented (e.g., thermal processes leading to singlet O_2 or to chemiluminescent substances), it is unusual and deserves further comment.

Two-Transition-State Hypothesis

If the transition states leading to S_π and S_σ had identical structures, there would be no way to explain the formation of the high-energy intermediate. The transition state for 1° R + NBS → RBr + S_π must have a higher energy than the transition state for 1° R + NBS → RBr + S_σ. This reasoning had led to the postulation of two transition states:[1,2]



The out-of-plane attack by X· involves the π electrons of the imide system and leads to the formation of S_π; the in-line attack perturbs the σ electrons of the N–Br bond and leads to the formation of S_σ. The two schemes in Figure 2 give a consistent picture for generation of succinimidyl radicals (σ and π) from the reactions of NBS with a variety of radicals. These schemes are in accord with the known chemistry of this system.

Scheme I (Figure 2) describes the NBS–Br_2 system. The reaction of Br· + NBS produces Br_2 + S_π in a near-thermoneutral step (solid path). On energetic grounds alone, the pathway producing the higher energy S_σ is too endothermic to contribute significantly in the chain sequence of this system. The absence of BPI production and a distinctive set of H-abstraction selectivities[1,2] are evidence for S_π as the exclusive succinimidyl chain carrier in the system in which Br_2 is present.

Scheme II (Figure 2) describes the system in which Br_2 is scavenged, thus making the relatively exothermic reaction of a primary alkyl radical with NBS the chain-propagating step for succinimidyl regeneration (R· of Scheme II). The activation energy involved in producing S_σ (solid path) must be less than that needed to produce S_π (dashed path). The following observations clearly suggest that S_σ is the sole succinimidyl intermediate involved in the system in which the Br_2-scavenging alkene is present: (a) BPI is formed as the major product, in some instances with >96% conversion,[3] and (b) reaction products indicates a strikingly different set of H-abstraction selectivities[1,2] than those observed for the NBS–Br_2 system.

The two schemes in Figure 2 exemplify in detail the hypothesis of two transition states required to rationalize succinimidyl radical chemistry.

Strategy for Testing the Two-Transition-State Hypothesis. A critical test of this hypothesis involves the introduction of different substrates (RH) into the NBS–alkene system, which upon reaction with succinimidyl form radicals of progressively greater stability

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Table I. Estimated ΔH Values for R· + NBS → RBr + S_π[a]

R·	D(R-Br)[b]	$-\Delta H$[b,c]	ref
1° R·	68.0	21.7	6
2° R·	68.0	21.7	6
Cl_2CH·	65.7[d]	19.4	6-8
3° R·	64.0	17.7	6
Cl_3C·	55.7	9.4	9
CH_2=$CHCH_2$·	54.3[d,e]	8.0	6, 8, 10
cyclohexadien-1,3-ylic-5	49.3[d,f]	3.0	6, 11
Br·	46.3	0.0	12

[a] Obtained from the difference of D(N-Br) of NBS (~46 kcal/mol)[4] and D(R-Br). [b] kcal/mol. [c] These values can be read as ΔH values since Skinner estimates the ΔH for the Br· + NBS reaction to be zero.[4] [d] Determined by the equation ΔH_f°(R·) + ΔH_f°(Br·) − ΔH_f°(RBr). [e] A bond dissociation energy for 3-bromocyclohexene of 56 kcal/mol is calculated similar to that described in footnote *f*, except that the value for ΔH_f°(cyclohexen-3-yl) of 30 kcal/mol (see ref 11) is uncertain. This value is not a reasonable one since an R-Br bond weaker than the allyl bromide bond is expected. [f] The ΔH_f° (R - Br) is calculated by using a value of +1.5 kcal/mol to convert C-H to C-Br (ref 6, pp 272, 280).

(Scheme II, R′·, R″·, R‴·). The heats of reactions associated with the attack of these alkyl radicals on NBS will decrease with increasing stability of the radical. This gradual change in energetics might affect the activation energies as shown by the solid and dashed paths in Scheme II. In this scheme, radicals above R″· will react with NBS to produce S_σ; radicals below R″· react with NBS to produce S_π (solid paths). The radicals near R″· should react with NBS to give a mixture of S_σ and S_π.

Estimated ΔH values for reactions of a variety of alkyl radicals with NBS are given in Table I.

Since there is a probe for S_σ, it is possible to test this hypothesis. The S_σ radical undergoes a reversible ring opening to ·$CH_2CH_2C(O)NCO$ (PI), which is effectively trapped by NBS to produce $BrCH_2CH_2C(O)NCO$ (BPI). The S_π radical does *not* undergo this ring-opening reaction.

The events that account for product formation in an S_σ system (NBS, alkene, CH_2Cl_2 solvent) are given in Scheme III. The rate of the interconversion $S_\sigma \rightleftarrows$ PI is closely competitive with abstraction of hydrogen from substrate.[3,13] The reactions (enclosed in the box) responsible for the formation of BPI (path a plus c) and the formation of $BrCHCl_2$ (path d) are in competition. Reactions outside the box, for example, reactions with additional substrate (path e), should have no influence on the competition within the box if S_σ is the sole succinimidyl involved. This scheme requires that if the initial [NBS] and [CH_2Cl_2] are kept constant for a series of experiments with different added substrates, the mole ratio $BrCHCl_2$/BPI (paths d/c) will remain constant regardless of how much S_σ is drained off by parasitic reactions, such as with RH.

The reaction conditions for testing this scheme were met by saturating CH_2Cl_2 solvent (78 mmol) with NBS (1.69 mmol, [NBS] = 0.22 M). The addition of small amounts of 1,1-dichloroethylene (0.07 M) to the solution scavenged adventitious bromine. Various substrates were present at concentrations from 0.20 to 0.78 M. The reactions were degassed and then irradiated at ~15 °C through Pyrex with a medium-pressure mercury arc. Internal standards were used to obtain absolute yields of products, utilizing a combination of gas chromatography and ^{1}H NMR. All analytical signals were accounted for by starting materials, products, $BrCHCl_2$, BPI, brominated substrates, and succinimide.

Reactions of NBS with ·$CHCl_2$ and 1° and 2° Alkyl Radicals. The validity of Scheme III was examined by studying the reactions without added substrates and with the addition of the substrates neopentane, *n*-butane, or cyclopentane, which serve to introduce ·$CHCl_2$ and 1° and 2° alkyl radicals into the systems (Table II).

In spite of substantial and variable diversion of the succinimidyl radicals into reactions with the added hydrocarbons, the fraction $BrCHCl_2$/BPI remained constant at ca. 0.022 ± 0.003, independent of the concentration of the added hydrocarbons (0.20–0.73 M).

Table II. Reactions[a] with Neopentane, *n*-Butane, and Cyclopentane

expt	substrate (M)[b]	products (mmol)	$BrCHCl_2$/BPI[c]
1	CH_2Cl_2 (15.6) CH_2CCl_2 (0.075)	BPI (1.65) $BrCHCl_2$ (0.039) succinimide (0.039)	0.024
2	CH_2Cl_2 (15.3) neo-C_5H_{12} (0.20) CH_2CCl_2 (0.074)	BPI (1.58) $BrCHCl_2$ (0.033) neo-$C_5H_{11}Br$ (0.041) succinimide (0.075)	0.021
3	CH_2Cl_2 (15.0) neo-C_5H_{12} (0.38) CH_2CCl_2 (0.072)	BPI (1.56) $BrCHCl_2$ (0.031) neo-$C_5H_{11}Br$ (0.079) succinimide (0.110)	0.020
4	CH_2Cl_2 (14.2) neo-C_5H_{12} (0.73) CH_2CCl_2 (0.068)	BPI (1.52) $BrCHCl_2$ (0.031) neo-$C_5H_{11}Br$ (0.139) succinimide (0.170)	0.020
5	CH_2Cl_2 (15.0) *n*-butane (0.38) CH_2CCl_2 (0.072)	BPI (1.47) $BrCHCl_2$ (0.030) 1-bromobutane (0.034) 2-bromobutane (0.077) succinimide (0.140)	0.021
6	CH_2Cl_2 (14.2) *n*-butane (0.73) CH_2CCl_2 (0.068)	BPI (1.37) $BrCHCl_2$ (0.029) 1-bromobutane (0.081) 2-bromobutane (0.186) succinimide (0.300)	0.021
7	CH_2Cl_2 (15.0) cyclopentane (0.38) CH_2CCl_2 (0.072)	BPI (1.41) $BrCHCl_2$ (0.035) cyclopentyl bromide (0.25) succinimide (0.275)	0.025

[a] 5.0 mL of CH_2Cl_2, 1.69 mmol of NBS. [b] Moles per liter. [c] Mole ratio.

Earlier work established that S_π reacts with CH_2Cl_2 to produce $BrCHCl_2$[2] without ring opening of the S_π. If the reaction of any R· with NBS had led to RBr and S_π, the fraction $BrCHCl_2$/BPI would have increased from the value observed when no additional substrate was present; in the limit, the fraction would go to infinity for a pure S_π system since S_π does not lead to BPI. Consequently, Scheme III is confirmed in detail with experiments 1-7. The alkyl radicals ·$CHCl_2$, 1° R, and 2° R, as well as the 1° radical PI, react with NBS to produce S_σ exclusively.

The addition of S_σ to 3,3-dimethyl-1-butene produces a 2° alkyl radical intermediate. In work reported elsewhere,[3] 3,3-dimethyl-1-butene was used as the added substrate at concentrations of from 0.029 to 0.282 M,[14] resulting in diversions (up to 20%) of NBS to the 1:1 NBS–olefin adduct, without significantly altering the $BrCHCl_2$/BPI ratio from the 0.022 value.

$$Cl_2CH\cdot + NBS \rightarrow RBr + S_\sigma$$

$$1^\circ\ R\cdot + NBS \rightarrow RBr + S_\sigma$$

$$2^\circ\ R\cdot + NBS \rightarrow RBr + S_\sigma$$

Reactions of NBS with Weaker Radicals. Shceme III is no longer valid if the added substrates, upon reaction with succinimidyl, produce radicals that are 3°, allylic, or cyclohexadienylic, such as isobutane, 2,3-dimethylbutane, cyclohexene, or benzene (Table III). In experiments 8–16, the $BrCHCl_2$/BPI ratios are larger than 0.022, the value characteristic of a pure S_σ system.

Unfortunately, systems containing these substrates are not homogeneous in the sense that they contain a number of different reactive centers, thus leading also to 1° and 2° alkyl radicals and ·$CHCl_2$, which produce S_σ on reaction with NBS. Nonetheless, in the presence of these substrates there is a loss of BPI relative to $BrCHCl_2$, a result that can be explained only if mixtures of S_σ and S_π were produced in the chain sequences (path e leading

(14) For example, in the case of 3,3-dimethyl-1-butene (0.282 M), the products are BPI (1.11 mmol), $BrCHCl_2$ (0.024 mmol), and *N*-(2-bromo-3,3-dimethyl-1-butyl)succinimide (0.32 mmol); see ref 3.

Table III. Reactions[a] with Isobutane, 2,3-Dimethylbutane, Cyclohexene, and Benzene

expt	substrate (M)[b]	products (mmol)	$BrCHCl_2$/BPI[c]
8	CH_2Cl_2 (15.0) isobutane (0.38) CH_2CCl_2 (0.072)	BPI (1.35) $BrCHCl_2$ (0.050) isobutyl bromide (0.084) *tert*-butyl bromide (0.133) succinimide (0.265)	0.037
9	CH_2Cl_2 (14.9) 2,3-dimethylbutane (0.38) CH_2CCl_2 (0.071)	BPI (1.25) $BrCHCl_2$ (0.056) 1-bromo-2,3-dimethylbutane (0.079) 2-bromo-2,3-dimethylbutane (0.21) succinimide (0.35)	0.045
10	CH_2Cl_2 (15.0) cyclohexene (0.38) CH_2CCl_2 (0.072)	BPI (0.62) $BrCHCl_2$ (0.045) 4-bromocyclohexene (0.022) 3-bromocyclohexene (0.110) 1-bromo-2-succinimidylcyclohexane (0.77) succinimide (0.18)	0.073
11	CH_2Cl_2 (15.3) benzene (0.20) CH_2CCl_2 (0.094)	BPI (0.71) $BrCHCl_2$ (0.10) *N*-phenylsuccinimide (0.14) succinimide (0.32) 1,2-dibromo-1,1-dichloroethane (0.15)	0.138
12	CH_2Cl_2 (15.0) benzene (0.40) CH_2CCl_2 (0.092)	BPI (0.34) $BrCHCl_2$ (0.10) *N*-phenylsuccinimide (0.14) succinimide (0.31) 1,2-dibromo-1,1-dichloroethane (0.14)	0.294
13	CH_2Cl_2 (14.5) benzene (0.78) CH_2CCl_2 (0.11)	BPI (0.23) $BrCHCl_2$ (0.14) *N*-phenylsuccinimide (0.15) succinimide (0.28) 1,2-dibromo-1,1-dichloroethane (0.15)	0.609
14	CH_2Cl_2 (11.5) benzene (2.47) 3,3-dimethyl-1-butene (0.34)	BPI (<0.09)[d] $BrCHCl_2$ (0.20) *N*-phenylsuccinimide (0.34) *N*-(2-bromo-3,3-dimethyl-1-butyl)-succinimide (0.12) succinimide (0.58) 1,2-dibromo-3,3-dimethylbutane (0.33)	>2.2[e]
15	CH_2Cl_2 (10.7) benzene (2.30) neo-C_5H_{12} (0.55) 3,3-dimethyl-1-butene (0.32)	BPI (<0.09)[d] $BrCHCl_2$ (0.13) neo-$C_5H_{11}Br$ (0.040) *N*-phenylsuccinimide (0.28) *N*-(2-bromo-3,3-dimethyl-1-butyl)-succinimide (0.11) succinimide (0.46) 1,2-dibromo-3,3-dimethylbutane (0.28)	>1.4[e]
16	CH_2Cl_2 (11.5) benzene (2.47) 1,3-butadiene (0.35) CH_2CCl_2 (0.094)	BPI (<0.09)[d] $BrCHCl_2$ (0.070) *N*-phenylsuccinimide (0.070) 1,3-butadiene addition products (1.23) succinimide (0.14)	>0.78[e]

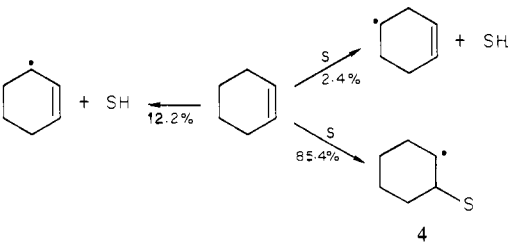
[a] 5.0 mL of CH_2Cl_2, 1.69 mmol of NBS. [b] Moles per liter. [c] Mole ratio. [d] No BPI was detected. [e] The minimum value reflects the detection limit for BPI.

to pure S_π or a mixture of S_π and S_σ). The introduction of S_π into the system by way of path e adds an alternate route to $BrCHCl_2$, without perturbing the competition within the box in Scheme III. The result is an increase in the $BrCHCl_2$/BPI mole ratio.

Reactions of NBS with 3° Alkyl Radicals. In experiments 8 and 9, NBS is subjected to attack by 3° as well as 1° alkyl radicals. The increase in the $BrCHCl_2$/BPI ratio must be attributed to the presence of 3° alkyl radicals. Further, the value of this fraction increases as the ratio of 3° to 1° hydrogens increases in going from isobutane to 2,3-dimethylbutane.

Reactions of NBS with Allylic Radicals. Scheme IV gives the reaction pathways observed in experiment 10 (cyclohexene as added substrate). Hydrogen abstractions from both the 4- and 3-positions generate the 4-cyclohexenyl (2°) and 3-cyclohexenyl (allylic) radicals, respectively. Succinimidyl radicals add readily to certain olefins,[15] this being the predominant reaction path

Scheme IV



4

observed with cyclohexene, generating the 2° alkyl radical **4**. Since 2° alkyl radicals react with NBS to produce S_σ exclusively, the increase in the fraction $BrCHCl_2$/BPI must be attributed to the reaction of NBS with the 3-cyclohexenyl radical, a pathway that accounts for only 7% of the NBS.

To study the influence of the allylic radical further, we examined succinimidyl addition to 1,3-butadiene. Addition of the succinimidyl to 1,3-butadiene results in the formation of an allylic radical

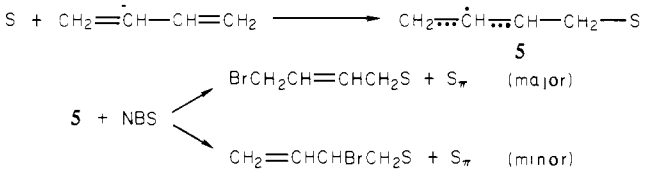
(15) Skell, P. S.; Day, J. C.; Katsaros, M. G.; Kocher, W. D.; Scott, A. E. *J. Am. Chem. Soc.* **1978**, *100*, 1950.

Table IV. Reactions[a] with 1,3-Butadiene

products (mmol)	substrates: CH_2=CHCH=CH_2 (2.0 mmol, 0.38 M)[b]	substrates: CH_2=CHCH=CH_2 (2.4 mmol, 0.44 M) + $(CH_3)_3$CCH=CH_2 (2.0 mmol, 0.36 M)
BPI	<0.09[c]	0.22
$BrCHCl_2$	0.029	0.020
$BrCH_2CH$=$CHCH_2S$ + CH_2=$CHCHBrCH_2S$	0.95	0.86
$(CH_3)_3CCHBrCH_2S$		0.10

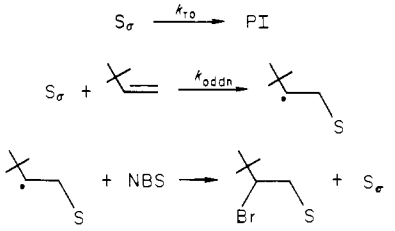
[a] 1.69 mmol of NBS, 78.1 mmol of CH_2Cl_2 (solvent). [b] 1,1-dichloroethylene present at 0.075 M. [c] Detection limit.

intermediate (**5**), which is subsequently trapped by NBS to give predominantly the 1,4 adduct.



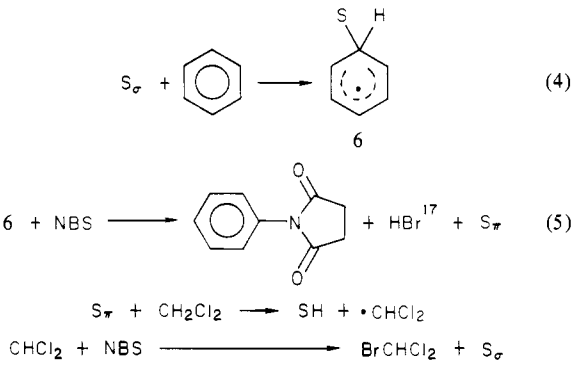
A reaction carried out with 1,3-butadiene as the added substrate (0.38 M), under the identical conditions as above, produces addition products (1,2 and 1,4), a small amount of $BrCHCl_2$, and no BPI (Table IV).

The absence of BPI in the 1,3-butadiene reaction can be interpreted as follows: (1) it is a pure S_π system or (2) 1,3-butadiene reacts rapidly enough with S_σ to preclude ring opening. The latter explanation can be rejected, since addition of 3,3-dimethyl-1-butene to the above reaction mixture results in significant BPI formation, along with the formation of NBS adducts from both of the olefinic substrates (Table IV). For reactions with NBS in the presence of olefins such as 3,3-dimethyl-1-butene (or ethylene), addition occurs with $k_{addn}/k_{ro} = 0.59$,[3] so that ring opening of S_σ and addition of S_σ to 3,3-dimethyl-1-butene are closely competitive pathways. The results of the experiment with both 3,3-dimethyl-1-butene and 1,3-butadiene present indicate



that the rates of addition of S_σ to these olefins are similar[16] and that the rate of S_σ addition to 1,3-butadiene is not so fast as to preclude ring opening of S_σ to PI. Consequently, the absence of BPI when 1,3-butadiene alone is present must be attributed to the reactions of allylic radical **5** with NBS producing exclusively S_π.

Scheme V



Reactions of NBS with Cyclohexadienylic Radicals. In experiments 11–13 (Table III) with benzene as the added substrate, the products attributed to reactions of succinimidyl are $BrCHCl_2$, BPI, and *N*-phenylsuccinimide.[1,14] A characteristic of these systems is that the ratio $BrCHCl_2$/BPI is much larger than the value of 0.022 for a pure S_σ system. The observed increase in the ratio must be caused by the generation of S_π in the system. However, it will be shown (vide infra) that S_π does not add to benzene, so that to continue the chain it is necessary to have present another substrate that can react readily with S_π and thus ultimately regenerate S_σ. For experiments 11–13, methylene chloride serves as this intermediary, and this explains the ratio of *N*-phenylsuccinimide to $BrCHCl_2$ being approximately 1.0. A reasonable candidate for the production of S_π is the cyclohexadienyl radical intermediate **6** (Scheme V). In experiments 14 and 15, 3,3-dimethyl-1-butene and neopentane react with S_σ to form 2° and 1° alkyl radicals, respectively, and these in turn regenerate S_σ upon reaction with NBS. In these experiments, the *N*-phenylsuccinimide yields are equal to the sum of the yields of $BrCHCl_2$, neopentyl bromide, and the NBS adduct of 3,3-dimethyl-1-butene. Unlike the experiments described in Table II (where the value of the ratio $BrCHCl_2$/BPI is independent of the substrate concentration), in experiments with benzene this ratio depends on the substrate concentration (the ratio increases with increasing benzene concentration). However, the ratio of all the brominated products ($BrCHCl_2$, neopentyl bromide, and *N*-(2-bromo-3,3-dimethyl-1-butyl)succinimide) to the *N*-phenylsuccinimide remains 1.0. This dependence on the benzene concentration is consistent with (a) a rapid addition of S_σ to benzene and (b) the reaction of NBS with cyclohexadienylic radical intermediate **6**, producing S_π (reaction 5). The S_π continues the chain by reacting with the other substrates that are present. In experiments 11–13, most of the $BrCHCl_2$ produced comes from the reaction of CH_2Cl_2 with S_π; only a minor amount (0.022 × BPI) comes from the reaction with S_σ. Since benzene is an efficient trap for S_σ, the mole ratio $BrCHCl_2$/BPI increases as the benzene concentration is increased. In experiments 14 and 15, the benzene concentrations are high enough to reduce the BPI concentration to below the detection limit. Under conditions where all S_σ is trapped by benzene, experiments 14 and 15, brominated substrates must come from the reaction of these substrates with S_π only. This is precisely what is observed in experiment 15: the relative rate ratio $(k_{neo\text{-}C_5H_{12}}/k_{CH_2Cl_2})_H$ is characteristic of a pure S_π attack on these substrates, being equal to 1.04 (the value of this relative rate ratio, per hydrogen, is 1.0 ± 0.10 for S_π and 17 ± 2 for S_σ).[1-3] These results suggest that in experiments 14 and 15 the additions to 3,3-dimethyl-1-butene should be attributed totally to S_π. Results to be presented elsewhere confirm this tentative suggestion.

A benzene–butadiene–CH_2Cl_2 reaction mixture (experiment 16) does not produce enough S_σ to make formation of *N*-phenylsuccinimide a major reaction channel, as does 3,3-di-

(16) In the absence of 1,3-butadiene (1,3-bu), 3,3-dimethyl-1-butene (3,3-Me_2-1-bu) reacts by a pure S_σ chain, giving BPI and *N*-(2-bromo-3,3-dimethyl-1-butyl)succinimide in a ratio of 2.5:1 when 3,3-dimethyl-1-butene and NBS are present at the same concentrations as in the 1,3-butadiene competition. Thus, in the competition with 1,3-butadiene, the amount of the 3,3-dimethyl-1-butene adduct resulting from S_σ addition is 0.22/2.5 = 0.088 mmol. Consequently, 0.012 mmol of the 3,3-dimethyl-1-butene adduct results from S_π addition. It will be shown elsewhere that the ratio of rate constants for addition of S_π is $(k_{1,3\text{-bu}}/k_{3,3\text{-Me}_2\text{-1-bu}})_{S_\pi} = 32.6$. Thus, the amount of 1,3-butadiene adducts from S_π addition is 0.012 × 32.6 × (2.4/2.0) = 0.47 mmol, leaving 0.39 mmol for S_σ addition. From this treatment, a relative rate for S_σ additions to this pair of olefins can be derived:

$$(k_{1,3\text{-bu}}/k_{3,3\text{-Me}_2\text{-1-bu}})_{S_\sigma} = \frac{0.39}{0.088} \times \frac{2.0}{2.4} = 3.7$$

(17) Hydrogen bromide is trapped rapidly by an ionic reaction with NBS to produce Br_2 and succinimide (Shea, K. J.; Lewis, D. C.; Skell, P. S. *J. Am. Chem. Soc.* **1973**, *95*, 7768–7776 and earlier references therein). The reaction of Br_2 with alkene yields 1,2-dibromoalkane, the amount being equal to that of the *N*-phenylsuccinimide.

methyl-1-butene (experiment 10), even though 1,3-butadiene is only 4 times more reactive than 3,3-dimethyl-1-butene in adding S_σ. The failure to form *N*-phenylsuccinimide in experiment 16 is attributed to the pure S_π chain propagated by the 1,3-butadiene.

In summary, allylic and cyclohexadienylic radicals react with NBS to produce S_π exclusively. While the results of experiments

$$\text{allylic}\cdot \text{ or cyclohexadienylic}\cdot + \text{NBS} \rightarrow \text{RBr} + S_\pi$$

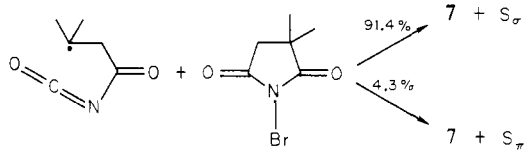
8 and 9 clearly indicate that the reactions of a 3° alkyl with NBS produce some S_π, the amount of reaction by this channel may be

$$3^\circ\ \text{R}\cdot + \text{NBS} \rightarrow \text{RBr} + S_\sigma + S_\pi$$

small. The next section lifts this ambiguity.

Reaction of NBS with a 3° Alkyl Radical: 2,2-Me_2NBS. Although it is evident that some S_π is produced in the reaction of NBS with a 3° alkyl radical, this appears to be a minor pathway since the ratio $BrCHCl_2$/BPI is only slightly elevated from the value for a pure S_σ system. Obtaining a better estimate from these reaction systems is probably not practicable without knowledge of the relative rates of the reactions of S_π and S_σ with each type of C–H bond in the system. For this reason, a different method was employed to examine the S_π to S_σ proportions resulting from the reaction of 3° alkyl radical with NBS.

When a reaction mixture of 2,2-Me_2NBS (1.45 mmol) in CH_2Cl_2 (78 mmol) containing neopentane (4.0 mmol) and 1,1-dichloroethylene (0.06 M) is irradiated to complete conversion, the products are 3-bromo-3-methylbutanoyl isocyanate (**7**) (1.39 mmol), $BrCHCl_2$ (0.046 mmol), neopentyl bromide (0.015 mmol), and 2,2-dimethylsuccinimide (0.062 mmol). The progenitors of the bromodichloromethane and neopentyl bromide become apparent when the ratio of their formation is examined. This rate ratio (per H) is 1.1, characteristic of S_π reactions with methylene chloride–neopentane mixtures (1.0 ± 0.1 for S_π). These products, the result of S_π reactions with substrates, account for 4.3% of the *N*-bromo imide. Since it has been shown that only S_σ converts to acyl isocyanates, it follows that 95.7% of the 2,2-dimethylsuccinimidyl radicals were produced in the σ state. A part of these σ radicals (4.3%) comes from the reactions of the *N*-bromo imide with $\cdot CHCl_2$ and neo-$C_4H_9\cdot$; the remainder (91.4%) must come from the reaction of the open-chain 3° radical with the *N*-bromo imide. It is assumed that this partitioning between π and σ is also quantitatively characteristic of all 3° alkyl radicals.



Since NBS and alkyl-substituted NBS react at the same rate in trapping alkyl radicals,[13,18] the following describes the reactions of NBS with tertiary alkyl radicals:

$$3^\circ\ \text{R}\cdot + \text{NBS} \xrightarrow{95.5\%} 3^\circ\ \text{RBr} + S_\sigma \qquad \Delta H = ?$$

$$3^\circ\ \text{R}\cdot + \text{NBS} \xrightarrow{4.5\%} 3^\circ\ \text{RBr} + S_\pi \qquad \Delta H = -17.7\ \text{kcal/mol}$$

If, as seems reasonable, no endothermic steps are involved in forming S_σ, then the reaction leading to S_σ is approximately thermoneutral, and $H_{S_\sigma} - H_{S_\pi} \approx 17.7$ kcal/mol; this value defines the upper limit for the enthalpy separation.

Reactions of NBS with Br· Radical. Earlier it was reported[1-3] that reaction mixtures of NBS in methylene chloride with molecular bromine present at concentrations greater than 10^{-3} M led to the formation of brominated substrate uncontaminated by BPI (Table V). This system required a mechanism in which bromine atom reacted with NBS and in which (a) the substrate radical is trapped by Br_2 instead of NBS and (b) S_π is the sole

Table V. Reaction[a] with Molecular Bromine

expt	substrate (M)[b]	products (mmol)	$BrCHCl_2$/BPI[c]
17	CH_2Cl_2 (15.6) Br_2 (>10^{-3})	$BrCHCl_2$ (0.50) succinimide (0.50)	>5.0[d]

[a] 5.0 mL of CH_2Cl_2, 1.69 mmol of NBS. [b] Moles per liter. [c] Mole ratio. [d] No BPI was detected. The minimum value reflects the detection limit for BPI, 0.09 mmol.

Table VI. Reaction[a] with Chloroform as Solvent

expt	substrate (M)[b]	products (mmol)	$BrCCl_3$/BPI[c]
18	$CHCl_3$ (12.4) CH_2CCl_2 (0.08)	$BrCCl_3$ (0.60) succinimide (0.60)	>5.00[d]

[a] 5.0 mL of $CHCl_3$, 1.69 mmol of NBS. [b] Moles per liter. [c] Mole ratio. [d] No BPI was detected. The minimum value reflects the detection limit for BPI, 0.09 mmol.

succinimidyl present, formed by the reaction of NBS with Br· (reaction 2). There are several independent lines of evidence that

$$S_\pi + CH_2Cl_2 \rightarrow SH + \cdot CHCl_2$$

$$\cdot CHCl_2 + Br_2 \rightarrow BrCHCl_2 + Br\cdot$$

$$Br\cdot + \text{NBS} \rightarrow Br_2 + S_\pi \qquad (2)$$

indicate that Br_2 is superior to NBS as a radical trapping agent,[1,19] and the absence of BPI indicates that only S_π is produced. This conclusion is consistent with the observation that no *N*-phenylsuccinimide is produced when benzene is present.

It was shown that if BPI had been produced, it would have survived the reaction conditions by demonstrating that (a) irradiation of a methylene chloride solution of Br_2 and BPI resulted in no loss of BPI and (b) added BPI survives unchanged in an experiment identical with experiment 17.

Reaction of NBS with $\cdot CCl_3$ Radicals. Another reaction that produces pure S_π is that of NBS with trichloromethyl radical. If chloroform is substituted for methylene chloride, serving as both solvent and substrate, no BPI is obtained; only $BrCCl_3$ and succinimide are produced in equimolar amounts. The reaction was carried out analogously to experiment 1, with 1,1-dichloroethylene present to scavenge any molecular bromine that developed. The result is given in Table VI.

It is remarkable that in shifting from CH_2Cl_2 to $CHCl_3$, as solvent and reactant, in the presence of 1,1-dichloroethylene, the

$$S_\pi + CHCl_3 \rightarrow SH + \cdot CCl_3 \qquad (6)$$

$$\cdot CCl_3 + \text{NBS} \rightarrow BrCCl_3 + S_\pi \qquad (7)$$

yield of BPI goes from 97.5% to 0. This is a result that can be understood with Scheme II (Figure 2), $\cdot CHCl_2$ + NBS above the changeover value and $Cl_3C\cdot$ + NBS below.

Addition of benzene (0.81 M) to the NBS–$CHCl_3$ system has no effect on the course of the reaction, the products being $BrCCl_3$ and succinimide uncontaminated by *N*-phenylsuccinimide. The failure of S_π to add to benzene is further demonstrated by this experiment. This experiment should be contrasted with experiment 13, identical except for methylene chloride solvent, in which *N*-phenylsuccinimide is the major product. *This minor change in the nature of the solvent could produce this dramatic effect only if $\cdot CHCl_2$ and $\cdot CCl_3$ give different products on reaction with NBS.*

Although chloroform would appear to be a solvent that would ensure S_π as the chain carrier, Johnson and Bublitz[20] reported good yields of BPI from NBS in chloroform solution *in the presence of allyl chloride*, evidence for S_σ involvement. Thus there appears to be an anomaly. We confirm this observation. The NBS–$CHCl_3$ system gives good yields of BPI in the presence of

(18) Martin, J. C., private communication.

(19) Tuleen, D. L.; Skell, P. S.; Readio, P. D. *J. Am. Chem. Soc.* **1963**, *85*, 2850.

(20) Johnson, H. W.; Bublitz, D. E. *J. Am. Chem. Soc.* **1958**, *80*, 3150.

3,3-dimethyl-1-butene; but there is no BPI in the presence of 1,1-dichloroethylene.

In the presence of 3,3-dimethyl-1-butene, both S_π and CCl_3 radicals are trapped by this alkene, leading to a 2° alkyl radical that reacts with NBS to form S_σ. The S_σ opens to PI and PI reacts with NBS to form BPI and S_σ, etc. Thus, the 3,3-dimethyl-1-butene scavenges the components that would make an S_π chain, exactly as in the Johnson and Bublitz experiment.

1,1-Dichloroethylene is apparently a poor trap for $\cdot CCl_3$ and S_π, so these radicals can carry on the S_π chain (eq 6 and 7).

An additional factor that accounts for good S_σ chains in the presence of $CHCl_3$ is the low rates of reaction of S_σ with chlorine-substituted methanes, $[k_{Me_4C}/k_{CH_2Cl_2}]_H = 17$; $CHCl_3$ is less reactive than CH_2Cl_2. On the other hand, for S_π, $[k_{Me_4C}/k_{CH_2Cl_2}/k_{CHCl_3}]_H = (1.0)/1.0/1.1$. Thus, S_σ chains are perpetuated because S_σ reacts poorly with $CHCl_3$; S_π chains are perpetuated because S_π reacts readily with $CHCl_3$ and thus regenerates S_π.

It is intriguing that S_π and S_σ chains operate independently in the same medium, crossovers occurring only with the aid of agents such as benzene, which reacts with S_σ but produces S_π, or CH_2Cl_2, which reacts with S_π or S_σ to produce $\cdot CHCl_2$, which in turn leads only to S_σ.

Concluding Remarks

The behavior of the succinimidyls produced in experiments 1–16 can be explained by using Figure 2 (Scheme II). Both 1° and 2° alkyl and $\cdot CHCl_2$ radicals react with NBS to produce S_σ exclusively. These reactions lie above the threshold for the changeover from S_σ to S_π. The reaction of NBS with allylic, cyclohexadienylic, trichloromethyl, and Br radicals lies below this threshold, producing solely S_π. The reaction of the 3° alkyl radical with NBS seems to be on the border between the two reaction domains. In summary:

$$\cdot CHCl_2,\ 1°\ R\cdot \text{ or } 2°\ R\cdot + NBS \rightarrow RBr + S_\sigma$$

$$3°\ R\cdot + NBS \rightarrow RBr + S_\sigma\ (95.5\%) + S_\pi\ (4.5\%)$$

$$\text{allylic}\cdot,\ \text{cyclohexadienylic}\cdot,\ Br\cdot,\ \text{or } CCl_3\cdot + NBS \rightarrow RBr + S_\pi$$

Two new systems for generating S_π, free of S_σ, have become available: (1) NBS–$CHCl_3$ in the presence of 1,1-dichloroethylene, which produces S_π only, and (2) NBS–CH_2Cl_2 with sufficient benzene to trap all the S_σ and produce S_π. The detailed examination of S_π chemistry will be reported elsewhere.

For reactions of R· with NBS, the concept of a high-energy route to S_σ and a low-energy route to S_π appears to be valid, and further, two distinctly different structures for the transition states leading to these succinimidyl radicals are required: an in-line structure for S_σ production and an out-of-plane structure for S_π are proposed. The reaction of 3° alkyl radical with NBS is on the border between these reaction domains, and this leads to the conclusion that $H_{S_\sigma} - H_{S_\pi} \leq 18$ kcal/mol.

The hypothesis that the selective conversions of NBS to S_π or S_σ involved out-of-plane and in-line transition states, respectively, which was proposed earlier,[1,2] may prove useful in extending the concepts to related systems.[1,21]

Although energetics alone may explain why stronger radicals react with NBS to produce S_σ and weaker ones S_π, Clark[22] has suggested an additional intriguing factor by pointing out that the in-line mode should be preferred by nucleophilic radicals and the out-of-plane mode by electrophilic radicals. Electron-transfer processes in the operation of these modes might be a concept nearly equivalent to Clark's suggestion.

Experimental Section

General. ^1H NMR spectra were recorded on a Varian EM-360 spectrometer with chemical shifts reported on the δ scale relative to Me_4Si. Infrared analyses were carried out on a Perkin-Elmer 580 or 727 spectrometer. Gas chromatography analyses were carried out on a Varian 1400 FID with a 60/80 Carbopak B 1% SP-1000 6 ft × 2 mm or a 100/120 Supelcoport 10% Silar 10 6 ft × 2 mm column. Mass spectra were taken on a Finnigan 3200 CI(CH_4) at low resolution or an AEI-MS 902 run at 70 eV.

Materials. *N*-Bromosuccinimide was obtained from Aldrich Chemical Co. The preparation of 2,2-dimethyl-*N*-bromosuccinimide has been described previously.[3] Methylene chloride was purified by successive extraction with concentrated H_2SO_4, distilled water, and 5% aqueous sodium bicarbonate solution, dried with anhydrous calcium chloride, and distilled from phosphorus pentoxide. Chloroform was purified by successive extraction with concentrated H_2SO_4 and distilled water, dried with anhydrous calcium chloride, and distilled from phosphorus pentoxide. 3,3-Dimethyl-1-butene and 1,1-dichloroethylene were obtained from Aldrich Chemical Co.; the former was used as received and the latter was vacuum distilled directly into the reaction vessel. The bromine employed in this work was Mallinckrodt Analyzed Reagent Grade and was used without further purification. Neopentane, Phillips (99%), was used without further purification. *n*-Butane and isobutane, Matheson (99%), were used as received. Cyclopentane and 2,3-dimethylbutane, Aldrich Chemical Co., were each distilled prior to use. Cyclohexene was obtained from J. T. Baker Chemical Co. and was distilled before use. Benzene was distilled (Na–K alloy) prior to use. 1,3-Butadiene was obtained from Matheson (99%) and dried with anhydrous $CaSO_4$ prior to use.

Photolysis Experiments. All reactions were carried out in 30-mL Pyrex pressure tubes sealed with Teflon (Du Pont fluorocarbon) needle valves. Reactant mixtures were degassed 3 times by a freeze–thaw technique, with freezing and evacuating at −196 °C and thawing at ambient temperature. The sealed pressure tube, in a Pyrex water-circulating bath maintained at 14–15 °C, was irradiated with a 400-W medium-pressure mercury arc.

Compositions of individual reaction mixtures are given in either Tables II–VI or the text. Irradiation times of 1.0–2.5 h were employed. Product yields were obtained from direct ^1H NMR integrations with an internal standard (hexamethyldisiloxane). Alternatively, yields of brominated substrates were determined by gas chromatography after addition of internal standard (chlorobenzene) and workup (aqueous $NaHSO_3$, aqueous $NaHCO_3$, and Na_2SO_4 drying). A third method involved the separation of the volatile and nonvolatile materials by vacuum trap-to-trap distillation (room temperature, 1 mm) into a −196 °C trap. The nonvolatile materials were analyzed by ^1H NMR and the volatile materials by GC without a workup. Products were identified by comparison of GC retention times and/or to spectra of authentic samples. Absolute product compositions for each experiment are given in Tables II–VI or the text. Detailed product analysis for analogous experiments have been described previously.[3]

β-Bromopropionyl isocyanate was prepared as an authentic sample by the procedure described by Johnson and Bublitz.[20] Pure β-bromopropionyl isocyanate was also isolated from product mixtures by vacuum trap-to-trap distillation (1 mm) at ambient temperature into a −10 °C trap (ethylene glycol–N_2): ^1H NMR ($CDCl_3$) AA′XX′ with triplets at δ 3.05, 3.55 (J = 1, 3 Hz, 4 H); IR (CH_2Cl_2, cm^{-1}) most prominent band at 2245 (s, NCO), 1735 (m), 1400 (m), 1070 (m). ^1H NMR integrations were used to determine the absolute yield in product mixtures.

***N*-Phenylsuccinimide** was prepared as an authentic sample by the condensation of succinic anhydride and aniline and subsequent recrystallization from absolute ethanol, mp 150–152 °C (lit.[23] mp 150 °C). Pure *N*-phenylsuccinimide was also isolated from the reaction of benzene with NBS by chromatographing the product mixture on neutral alumina (pentane–methylene chloride): mp 150–152 °C, undepressed by admixture with the authentic sample; ^1H NMR (CH_2Cl_2) δ 2.75 (s, 4 H), 7.05–7.5 (m, 5 H). ^1H NMR integrations were used to determine the absolute yield in product mixtures.

1-Bromo-2-succinimidylcyclohexane was isolated as a liquid from the reaction of cyclohexene with NBS by (a) removal of volatile materials in vacuo, (b) extraction of nonvolatile products with CCl_4, and (c) evaporation of CCl_4 in vacuo: ^1H NMR ($CDCl_3$) δ 1.15–2.1 (m, 8 H), 2.7 (s, 4 H), 3.8–5.0 (m, 2 H); MS (CI), m/e 260, 262 (1:1, $M^+ + H$), 180 (M + H − Br). H^1 NMR integrations were used to determine the absolute yield in product mixtures.

The addition products resulting from the experiments with 1,3-butadiene present were isolated by chromatographing the product mixture on silica gel (hexane–ethyl acetate).

1-Bromo-4-succinimidyl-2-butene: ^1H NMR ($CDCl_3$) δ 2.7 (s, 4 H), 3.3–4.4 (M, 4 H), 5.5–5.9 (m, 2 H); MS (CI), m/e 232, 234 (1:1, $M^+ + H$), 153 ($M^+ + H - Br$).

3-Bromo-4-succinimidyl-1-butene: ^1H NMR ($CDCl_3$) δ 2.8 (s, 4 H), 3.3–3.7 (m, 2 H), 5.5–5.9 (m, 3 H), 6.4–6.6 (m, 1 H). ^1H NMR integrations were used to determine the absolute yields in product mixtures.

***N*-(2-Bromo-3,3-dimethyl-1-butyl)succinimide** was isolated from product mixtures as described previously:[3] mp 84–86 °C; ^1H NMR

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(CCl_4) δ 1.1 (s, 9 H), 2.65 (s, 4 H), 3.6-4.4 (m, 3 H); MS (EI), *m/e* 261, 263 (1:1, M^+), 204, 206 (1:1, $M^+ - C_4H_9$), 182 ($M^+ - Br$). ^1H NMR integrations were used to determine the absolute yield in product mixtures.

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Registry No. Neopentane, 463-82-1; *n*-butane, 106-97-8; cyclopentane, 287-92-3; isobutane, 75-28-5; 2,3-dimethylbutane, 79-29-8; cyclohexane, 110-83-8; benzene, 71-43-2; 1,3-butadiene, 106-99-0; bromine, 7726-95-6; chloroform, 67-66-3; *N*-bromosuccinimide, 128-08-5; 1-bromo-2-succinimidylcyclohexane, 82469-57-6; 1-bromo-4-succinimidyl-2-butene, 82469-58-7; 3-bromo-4-succinimidyl-1-butene, 82469-59-8; *N*-(2-bromo-3,3-dimethyl-1-butyl)succinimide, 72323-45-6.

Polyether Biosynthesis. 2. Origin of the Oxygen Atoms of Monensin A

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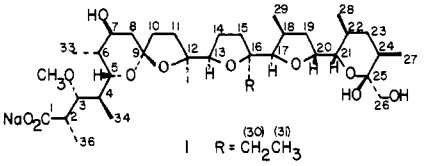
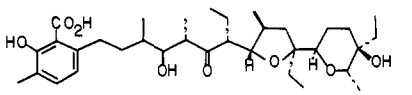
Abstract: Feeding of [1-^{13}C]acetate to cultures of *Streptomyces cinnamonensis* gave monensin A labeled at carbons 7, 9, 13, 19, and 25, as established by ^{13}C NMR analysis. Similarly, incorporation of [1-^{13}C]propionate resulted in enrichment of carbons 1, 3, 5, 11, 17, 21, and 23. Further incorporations of [1,2-$^{13}C_2$]acetate, [1,2-$^{13}C_2$]propionate, [2-^{13}C]propionate, and [2,3-$^{13}C_2$]succinate and analysis by ^{13}C NMR, including extensive homonuclear $^{13}C\{^{13}C\}$ decoupling, established the biosynthetic origins of all the carbon atoms of monensin, while allowing a complete assignment of the ^{13}C NMR spectrum. When [1-^{13}C,1-$^{18}O_2$]propionate was fed, isotopically shifted peaks indicating the presence of oxygen-18 at C-1, C-3, and C-5 were observed, whereas feeding of [1-^{13}C,1-$^{18}O_2$]acetate gave rise to excess oxygen-18 at C-7, C-9, and C-25. Three of the remaining ether oxygens, O(7), O(8), and O(9), were shown to be derived from molecular oxygen by growth of *S. cinnamonensis* in an atmosphere of $^{18}O_2$ and ^{13}C NMR analysis of the resulting labeled monensin A. These results are consistent with initial formation of the *all-E*-triene **7**, which can be converted to monensin by cyclization of the triepoxide **8**.

The polyether antibiotics, a group of more than 60 naturally occurring ionophores,[2] have attracted intense chemical and biochemical attention since the determination of the structure of monensin A (**1**) only 15 years ago.[3] Two of these compounds, monensin and lasalocid (**2**),[4] have found important veterinary applications in the control of coccidiosis in poultry and as agents for the improvement of feed utilization in ruminant livestock. The

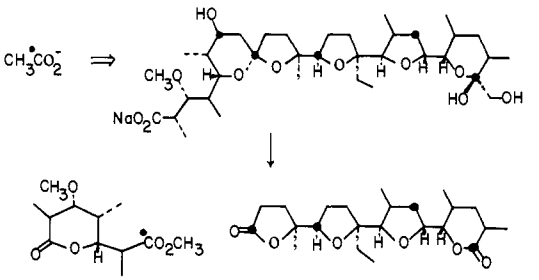


1 R = CH_2CH_3
6 R = CH_3



2

Scheme I



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vast majority of these polyoxygenated, branched-chain fatty acids are produced by species of the genus *Streptomyces*. Recent investigations in several laboratories of the biosynthesis of these substances have focussed on identification of the simple precursors acetate, propionate, and butyrate and suggested an analogy to the well-understood formation of saturated fatty acids as well as to the biosynthesis of a second major class of polyoxygenated *Streptomyces* metabolites, the macrolide antibiotics.[5] In our own work we have been interested in establishing the details of the pathways by which both macrolides[6] and polyethers are formed from their simple precursors. Our initial efforts have concentrated on determining the extent to which the implied analogy to classical fatty acid biosynthesis is in fact applicable to the formation of these functionally and stereochemically far more complex analogues. To address this question, we have recently determined the origin of the oxygen atoms of monensin, and our results are described below.[7]

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