= 20.4, 14.7 Hz), 3.35 (s, 1 H), 2.84–2.72 (m, 2 H), 2.20–2.08 (m, 2 H), 1.69 (dt, 1 H, J = 15.2, 2.5 Hz), 1.48–1.35 (m, 2 H), 1.27–0.80 (m, 2 H), 1.12 (d, 3 H, J = 7.0 Hz), 1.06 (s, 9 H), 0.97 (s, 3 H), 0.91 (d, 3 H, J = 5.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.24, 170.76, 154.93, 135.64, 135.46, 132.23, 132.13, 130.29, 128.07, 128.01, 91.51, 80.27, 78.29, 62.05, 47.81, 44.85, 43.82, 38.20, 36.70, 34.61, 33.94, 28.70, 28.17, 26.96, 24.86, 19.25, 18.82, 13.20, 12.21. An analytical sample was prepared by recrystallization from diethyl ether, mp 208–210 °C. Anal. Calcd for $C_{37}H_{46}O_8Si$: C, 68.70; H, 7.17. Found: C, 68.59; H, 7.13.

(1β,2α,12α)-20-(*tert*-Butyldiphenylsiloxy)-1,2,12-trihydroxypicrasane-11,16-dione (8). A solution of 128 mg (0.20 mmol) of cyclic carbonate 7 in 3.6 mL of methanol and 3.6 mL of tetrahydrofuran was treated at ambient temperature with 27 mg (0.20 mmol) of potassium carbonate. After 1 h, the reaction was acidified with 500 μL of a 10% aqueous hydrochloric acid solution. After being stirred for 30 min, the reaction contents were filtered through a pad of silica gel and washed successively with chloroform–methanol (9:1). The filtrate was concentrated in vacuo, and the product was chromatographed on 30 g of flash silica gel. Elution with chloroform–methanol (92:8) provided 107 mg (87%) of triol 8, which was recrystallized from acetone, mp 227–229.5 °C: R_f 0.18 (ethyl acetate); IR (KBr) 3524 (s), 3344 (s), 3255 (m), 3073 (w), 3048 (w), 2961 (s), 2939 (s), 2902 (m), 2858 (m), 1720 (s), 1693 (s), 1590 (w), 1474 (m), 1429 (m), 1390 (m), 1364 (m), 1342 (m), 1286 (m), 1268 (m), 1244 (m), 1226 (m), 1199 (w), 1165 (w), 1112 (s), 1065 (s), 1041 (s), 1019 (m), 993 (m), 959 (w), 943 (w), 928 (w), 822 (m), 803 (m), 772 (m), 743 (m), 703 (s), 689 (m), 618 (m) cm^{-1}; ^{1}H NMR (500 MHz, C_5D_5N) δ 8.13 (d, 1 H, J = 4.5 Hz), 7.81–7.73 (m, 4 H), 7.55–7.42 (m, 6 H), 5.73 (br s, 1 H), 5.32 (br s, 1 H), 5.05 (br s, 1 H), 4.24 (dd, 1 H, J = 17.7, 11.7 Hz), 4.20 and 4.01 (AB quartet, 2 H, J = 11.5 Hz), 4.12 (t, 1 H, J = 3.6 Hz), 4.04 (s, 1 H), 3.96–3.87 (m, 1 H), 3.35 (br d, 1 H, J = 8.4 Hz), 3.14–3.01 (m, 2 H), 2.41–2.32 (m, 1 H), 2.05 (dt, 1 H, J = 12.7, 4.0 Hz), 1.87 (d, 1 H, J = 13.4 Hz), 1.50–1.06 (m, 4 H), 1.37 (s, 3 H), 1.22 (d, 3 H, J = 6.9 Hz), 1.13 (s, 9 H), 0.75 (d, 3 H, J = 6.9 Hz); ^{13}C NMR (125 MHz, C_5D_5N) δ 213.39, 170.66, 136.14, 136.00, 135.81, 133.19, 133.14, 130.64, 130.60, 128.51, 128.45, 123.79, 86.34, 82.16, 79.05, 70.16, 62.85, 48.31, 46.03, 44.00, 43.22, 41.80, 35.88, 35.68, 29.05, 28.26, 27.12, 26.11, 19.63, 19.45, 13.86, 12.23; high-resolution MS (CI) calcd for $C_{32}H_{39}O_7Si$ (M – C_4H_9) m/e 563.2466, found 563.2477.

(±)-Shinjulactone D (1). To a solution of 97 mg (0.16 mmol) of silyl ether 8 dissolved in 3.1 mL of anhydrous tetrahydrofuran at room temperature was added 3.12 mL (3.12 mmol) of a 1.0 M solution of tetra-*n*-butylammonium fluoride in tetrahydrofuran. After being stirred for 3 h, the reaction contents were filtered through a pad of flash silica gel and washed successively with chloroform–methanol (9:1). The filtrate was concentrated in vacuo, and the resulting solid was chromatographed on 30 g of flash silica gel. Elution with ethyl acetate–methanol (8:1) afforded 54 mg (90%) of (±)-shinjulactone D, which upon recrystallization from acetone provided fine needles, mp 277–280 °C: R_f 0.29 (chloroform–methanol, 9:1); IR (KBr) 3500 (s), 3411 (s), 3261 (m), 2971 (m), 2933 (m), 2883 (m), 2786 (m), 2593 (w), 1725 (s), 1505 (m), 1470 (m), 1436 (m), 1409 (m), 1385 (m), 1343 (w), 1324 (m), 1293 (m), 1262 (m), 1235 (m), 1216 (m), 1177 (m), 1131 (w), 1081 (m), 1046 (s), 1011 (m), 984 (m), 961 (m), 945 (m), 918 (w), 884 (w), 857 (w), 795 (w), 764 (w), 718 (w), 633 (w), cm^{-1}; ^{1}H NMR (500 MHz, C_5D_5N) δ 6.87 (br d, 1 H, J = 4.5 Hz), 4.40 (br s, 1 H), 4.13 and 3.70 (AB quartet, 2 H, J = 8.1 Hz), 4.09–4.01 (m, 1 H), 3.95 (t, 1 H, J = 4.5 Hz), 3.58 (d, 1 H, J = 8.3 Hz), 3.27 (dd, 1 H, J = 18.5, 14.4 Hz), 2.95 (s, 1 H), 2.81 (dd, 1 H, J = 18.5, 5.5 Hz), 2.46–2.37 (m, 1 H), 2.08 (dt, 1 H, J = 12.7, 4.4 Hz), 1.94 (br d, 1 H, J = 14.5 Hz), 1.87 (dt, 1 H, J = 14.4, 5.5 Hz), 1.70 (t, 1 H, J = 14.4 Hz), 1.64 (s, 3 H), 1.59–1.49 (m, 1 H), 1.41 (t, 1 H, J = 11.7 Hz), 1.26 (q, 1 H, J = 12.2 Hz), 1.06 (d, 3 H, J = 6.8 Hz), 0.81 (d, 3 H, J = 5.9 Hz); ^{13}C NMR (125 MHz, C_5D_5N) δ 170.65, 110.90, 85.31, 79.70, 79.19, 71.75, 70.05, 46.53, 46.47, 44.19, 43.37, 42.90, 41.59, 31.70, 30.60, 29.01, 26.78, 20.10, 13.30, 11.61; high-resolution MS (CI) calcd for $C_{20}H_{31}O_7$ (M + 1) m/e 383.2070, found 383.2083; calcd for $C_{20}H_{29}O_6$ (M + 1 – H_2O) m/e 365.1965, found 365.1945.

Acknowledgment. Generous support for this work from the National Cancer Institute, National Institutes of Health (Grant CA 28865), is gratefully acknowledged. We are indebted to Professor Takahashi for providing us with the IR, ^{1}H NMR, and ^{13}C NMR spectra of natural shinjulactone D.

Registry No. (±)-1, 137175-14-5; (±)-3, 130575-39-2; (±)-4, 137175-15-6; (±)-5, 137175-16-7; (±)-6, 137175-17-8; (±)-7, 137175-18-9; (±)-8, 137175-19-0.

Approximate Absolute Rate Constants for the Reactions of Tributyltin Radicals with Aryl and Vinyl Halides

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Introduction

Rate constants of atom (and group) transfer reactions to tributyltin radicals are of fundamental interest in radical chemistry,[2] and they are also important in synthesis planning.[3] Such rate constants are used to determine at what concentrations a radical precursor will be reactive enough to propagate a good chain and to anticipate whether an atom or group transfer reaction will be faster or slower than other possible competing reactions. A large body of both absolute and relative rate data exists for tin radical abstractions of groups bonded to sp^3-hybridized carbon atoms.[2] In contrast, while it is well known that bromides and iodides bonded to sp^2-hybridized carbon atoms are useful radical precursors,[4] very little is known about the relative reactivity of these precursors. This absence of data threatened to impede several of our projects, so we undertook a brief study to determine the rate constants for bromine abstraction by tributyltin radical from a representative series of aryl and vinyl bromides and one aryl iodide. Finally, we provide illustrative applications of these rate constants to synthesis problems.

Results

Relative reactivities were measured by competition reactions of a known standard (R^2–Y) with a given radical precursor (R^1–X), as outlined in Scheme I. We selected

Scheme I

$$R^1\text{–}X + R^2\text{–}Y \xrightarrow{Bu_3SnH} R^1\text{–}H + R^2\text{–}H + Bu_3SnX(Y)$$

$$R^1\text{–}X + Bu_3Sn^\bullet \xrightarrow{k_X} R^{1\bullet} + Bu_3SnX$$

$$R^{1\bullet} + Bu_3SnH \rightarrow R^1\text{–}H + Bu_3Sn^\bullet$$

$$R^2\text{–}Y + Bu_3Sn^\bullet \xrightarrow{k_Y} R^{2\bullet} + Bu_3SnY$$

$$R^{2\bullet} + Bu_3SnH \rightarrow R^2\text{–}H + Bu_3Sn^\bullet$$

R^2–Y = 1-bromooctane, benzyl chloroacetate, or 4-bromoanisole

(1) Dreyfus Teacher–Scholar, 1986–91; National Institutes of Health Research Career Development Awardee, 1987–92.

(2) Leading references: (a) Ingold, K. U.; Lusztyk, J.; Scaiano, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 343. (b) Beckwith, A. L. J.; Pigou, P. *Aust. J. Chem.* **1986**, *39*, 77, 1151.

(3) (a) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon: Oxford, 1986. (b) Curran, D. P. *Synthesis* **1988**, 417, 489. (c) Curran, D. P. In *Comprehensive Organic Synthesis*; Pergamon: Oxford, 1991 (in press); Vol. 4, Chapter 4.1, 4.2. (d) Fevig, T. L.; Curran, D. P.; Jasperse, C. P. *Chem. Rev.*, in press.

(4) (a) Stork, G.; Baine, N. H. *J. Am. Chem. Soc.* **1982**, *104*, 2321. (b) Stork, G.; Baine, N. H. *Tetrahedron Lett.* **1985**, *26*, 5927. (c) Beckwith, A. L. J.; Gara, W. B. *J. Chem. Soc., Perkin Trans. 2* **1975**, 593, 795.

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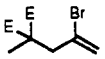
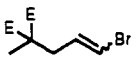
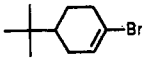
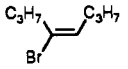
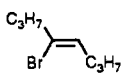
Table I. Relative Reactivity of =C—X Radical Precursors toward Tributyltin Radical

entry[a]	precursor[a]	standard[b]	k_{rel}	k (M^{-1} s^{-1}) (80 °C)
standard A	benzyl chloroacetate	-	1.38	3.3×10^6
standard B	1-bromooctane	-	15.2	5.8×10^7
1	4-*tert*-butyl-1-bromobenzene	A	1.00	2.4×10^6
2	4-iodoanisole	B	370	8.8×10^8
3	4-bromoanisole	A	1.00	2.4×10^6
4	3-bromoanisole	A	1.67	4.0×10^6[f]
5	2-bromoanisole	A	1.88	4.5×10^6
6	4-bromoacetophenone	C	1.63	3.9×10^6
7	3-bromoacetophenone	C	1.92	4.6×10^6
8	2-bromoacetophenone	C	6.70	1.6×10^7
9	4-bromobenzonitrile	C	2.83	6.8×10^6
10	3-bromobenzonitrile	C	3.75	9.0×10^6
11	2-bromobenzonitrile	C	6.67	1.6×10^7
12[d]		A	5.00	1.2×10^7
13[c,d]		A	0.45	1.1×10^6
14		A	1.42	3.4×10^6
15[e]		A	2.04	4.9×10^6
16[e]		A	0.54	1.3×10^6

[a] Entry number and number of precursor are the same. [b] A = benzyl chloroacetate; B = 1-bromooctane; C = 4-bromoanisole. [c] The precursor was a 2/3 mixture of *Z*/*E* vinyl bromides. The reported k is a composite. No effort was made to determine the relative reactivity of the individual isomers. [d] E = CO_2Et. [e] A 3/2 mixture of (*E*)- and (*Z*)-4-octene was formed. [f] This rate constant was also determined at 25 °C: $k = 7.1 \times 10^5$ M^{-1} s^{-1}.

1-bromooctane[5] and benzyl chloroacetate[6] as the two standards for these competitions because their relative reactivities toward tin radical were known and were in a convenient range and because the reduced products (octane and benzyl acetate) were readily quantified by GC. After completing an extensive series of competition experiments of these two standards with 4-bromoanisole, we then began to use 4-bromoanisole as a standard as well. Test radical precursors were selected because they were representative of common classes of aryl and vinyl halides or were relevant to specific problems in our group. Table I summarizes all the results.

In general, a degassed benzene solution of the test substrate (3 equiv, 1.5 M), the standard substrate (3 equiv), mesitylene (1 equiv, internal GC standard), AIBN (0.12 equiv), and tributyltin hydride (1 equiv) was immersed in an oil bath at 80 °C (± 3 °C) and heated for 4 h. The reaction mixture was cooled, and the ratio of the reduced test substrate to the reduced standard was determined by GC. Response factors for all reduced compounds and were used to correct the raw GC integrations to obtain accurate product ratios. Corrected product ratios were converted to relative reactivities by using standard kinetic equations for tin hydride competitions (see Experimental Section).[2b] Some test substrates were conducted with two standards, and at least two trials were run with each standard. Typical variation from standard to standard and trial to trial was less than 10%, so the average relative reactivities from several trials that are presented in Table I should be quite accurate. 4-*tert*-Butyl-1-bromobenzene is assigned a relative reactivity of 1, and we assume that its reactivity should be similar to that of bromobenzene. (This assumption could not be tested experimentally because benzene was the solvent.)[7] The absolute rate constants from Table I were calculated by using the Arhennius equation to extrapolate the known rate constants for reactions of 1-bromooctane[5] or benzyl chloroacetate[6] from 25 to 80 °C and then multiplying these values by the appropriate reactivity factor. The absolute rate constants in Table I are probably not highly accurate (any errors in the base rate constant are compounded by errors in our temperature conversion[5,6] and in our measurements); however, they are accurate enough for typical synthetic applications.

Table II. Reactivities of Selected Radical Precursors toward $Bu_3Sn^•$

k_X (M^{-1} s^{-1})	
$\geq 10^9$	alkyl iodides
10^8–10^7	alkyl bromides, aryl iodides
10^6–10^5	alkyl phenyl selenides, aryl bromides, vinyl bromides, α-chloro esters, α-thiophenyl esters
10^4–10^2	α-chloro and α-thiophenyl ethers, alkyl chlorides, alkyl phenyl sulfides

Discussion

The results in Table I can be used to calibrate the reactivity of aryl and vinyl halides relative to other known radical precursors. Table II provides an approximate scale of the reactivity of some representative atom and group donors toward tributyltin radicals. The relatively high reactivity of aryl bromides and iodides is striking in view of the increased energies of sp^2 C–X bonds compared to sp^3 C–X bonds. Aryl iodides are equalled as radical precursors only by reactive precursors like alkyl bromides and are exceeded only by alkyl iodides (which react with tin radicals at rates approaching the diffusion controlled limit). Even vinyl and aryl bromides have a good level of reactivity toward tributyltin radicals, and they are more reactive than many classes of chloride and phenyl selenide precursors of radicals.[2b]

Variations in reactivity within the series of aryl and vinyl bromides studied are rather small. The most reactive bromide, 2-bromobenzonitrile (entry 11), is only about 15 times more reactive than the least reactive, vinyl bromide 13 (a precursor of a primary vinyl radical, entry 13). Many of the observed trends are consistent with a small polar effect on the halogen abstraction reaction, as illustrated in eq 1.[8] The tributyltin radical bears a very slight positive

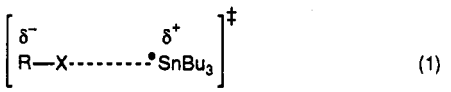
(5) The E_a (3.6 kcal/mol) for the reaction of primary alkyl bromides with tributyltin radical is reported in Cooper, J.; Hudson, A.; Jackson, R. A. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1056 and an accurate rate constant (2.6×10^7 M^{-1} s^{-1} at 25 °C) is reported in ref 2a. From these we can calculate that log $A \approx 10$, and that $k_{Br} = 5.8 \times 10^7$ M^{-1} s^{-1} at 80 °C.

(6) The rate constant for reaction of ethyl chloroacetate with $Bu_3Sn^•$ is reported in ref 2b. We assume that benzyl chloroacetate has the same rate constant as ethyl chloroacetate. Assuming that log $A = 9$ for this reaction (same log A as benzyl chloride), we calculate $E_a \approx 4.0$ kcal/mol and k_{Cl} at 80 °C.

(7) However, we can obtain an estimated rate constant for bromobenzene from literature data. At 80 °C, benzyl chloride has been reported to be 1.24 times more reactive than bromobenzene (Menapace, L. W.; Kuivala, H. G. *J. Am. Chem. Soc.* **1964**, *86*, 3047). By adjusting k_{Cl} for benzyl chloride to 80 °C (4.3×10^6 M^{-1} s^{-1}) and dividing by 1.24, we can obtain an estimate of k_{Br} for bromobenzene = 3.5×10^6 M^{-1} s^{-1}. This compares favorably with the measured k_{Br} for 4-*tert*-butyl-1-bromobenzene (Table I, entry 1).

(8) Polar effects: Zavitsas, A. A.; Pinto, J. A. *J. Am. Chem. Soc.* **1972**, *94*, 7390. Huyser, E. S. *Free Radical Chain Reactions*; Wiley Interscience: New York, 1970, p 77.

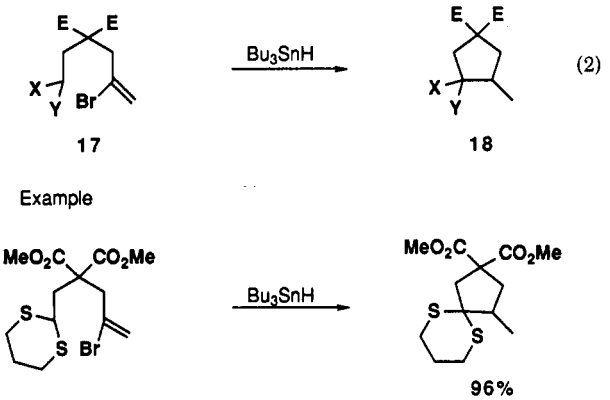
charge, and the substrate bears a very slight negative charge. This explains the general trend in increasing reactivity from 4-bromoanisole (1.0) < 4-bromoacetophenone (1.6) < 4-bromobenzonitrile (2.83) (compare entries 3/6/9). Comparison of the meta- or ortho-substituted series reveals similar trends (entries 4/7/10; 5/8/11). Holding the substituent constant but changing its location reveals a trend in increasing reactivity para < meta < ortho. This effect is also very small (a factor of 2 or 3), but it seems real because it appears for each of the three substituents (compare entries 3/4/5, 6/7/8, 9/10/11). This trend is probably not steric in origin. Perhaps it also reflects the polar effect in eq 1; bromine atoms closer to the inductive electron-withdrawing group are more reactive.



(1)

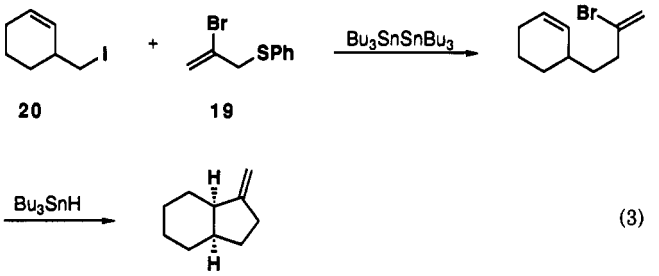
The reactivity of a simple vinyl halide like **14** (entry 14) is marginally higher than that of 4-*tert*-butyl-1-bromobenzene (1.4/1). Trends within the vinyl halide series can also be rationalized by using standard arguments. A precursor of a primary vinyl radical (entry 13) is about 5 times less reactive than precursors of secondary vinyl radicals (entries 14, 15). A precursor of a cyclic secondary radical (entry 14) is marginally less reactive than an appropriate acyclic *Z*-alkene counterpart (entry 16), perhaps due to a slight relief of strain in the transition state derived from the *Z*-alkene. Alkene **12** (entry 12) has inordinately high reactivity when compared to alkenes **14** and **15** (entries 14, 15), and this is probably due to the electronegative esters that are situated nearby. Finally, *Z*-alkene **16** has a decreased reactivity compared to *E*-alkene **15**, and this is probably due to unfavorable steric interactions between the approaching tin radical and the *Z* substituent. Indeed, there is some circumstantial evidence that very large rate differences between (*E*)- and (*Z*)-vinyl bromides will be observed if large alkene substituents are present.[9]

The rate constants aid in the planning of radical reactions where multiple radical precursors are present. Two examples of this are presented in eqs 2 and 3. Vinyl



(2)

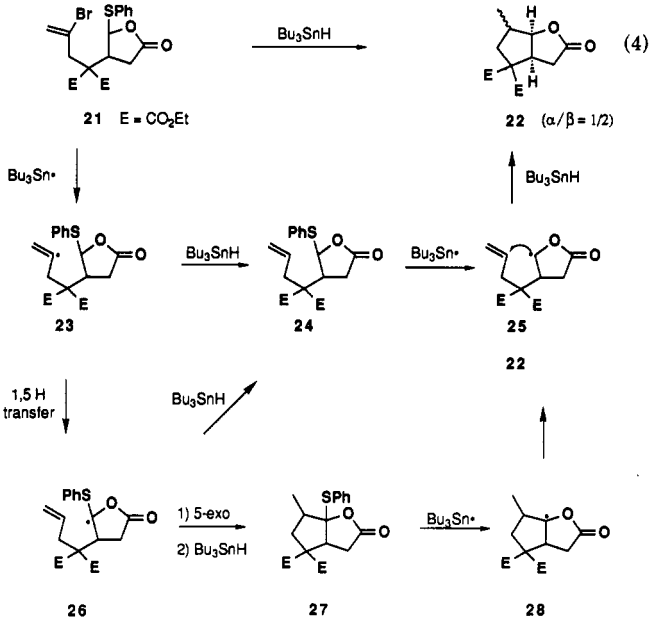
bromides like **17** are precursors for radical translocation,[10] but the transformation of **17** to **18** can succeed only if the vinyl bromide is a more reactive radical precursor than the groups X and Y. Groups (X, Y) containing sulfur are of special interest for preparative applications. Since many



(3)

sulfur-containing groups are less reactive radical precursors than vinyl bromides,[2b] they can be successfully incorporated into the radical translocation scheme without risk of reaction with tin hydride (provided that excess tin hydride is not used). In the contrast, eq 3 presents a reaction where the goal is to avoid initial generation of a radical from the vinyl bromide **19** and to have this group function as a radical acceptor. This can be accomplished provided that the radical donor **20** is highly reactive. Once the first radical allylation is complete, the vinyl radical can then be generated for use in a standard cyclization.[11]

The last example that we analyze is an interesting observation of Marino (Eq 4).[12] Reduction of **21** with 2 equiv of tributyltin hydride produced **22** in 87% yield. By comparing our rate data for vinyl bromides with Beckwith's rate data for some phenyl sulfides,[2b] we can conclude with a reasonable level of confidence that the vinyl bromide reacts with the first equivalent of tin hydride. The simplest sequence for formation of **22** is then initial conversion of **21** to **24**, followed by standard reductive cyclization (**24** → **25** → **22**). However, more intricate sequences involving 1,5-hydrogen transfer can also be envisioned,[10] as outlined in eq 4 (**21** → **23** → **26** → **24** or **21** → **23** → **26** → **27** → **28** → **22**). Sequences where the phenylthio group is the precursor of the first radical seem unlikely.



(4)

Experimental Section

General. All of the aryl halides were commercially available and most were used without further purification. The only exceptions were 3- and 4-bromoacetophenone, which required further purification by distillation or chromatography to remove colored

(9) Jasperse, C. P.; Curran, D. P. *J. Am. Chem. Soc.* **1990**, *112*, 5601.
(10) (a) Curran, D. P.; Kim, D.; Liu, H. T.; Shen, W. *J. Am. Chem. Soc.* **1988**, *110*, 5900. (b) Shen, W. Ph.D. Thesis, University of Pittsburgh, 1991.
(11) Jasperse, C. P.; Yoo, B.-W., unpublished results.
(12) Marino, J. P.; Laborde, E.; Paley, R. S. *J. Am. Chem. Soc.* **1988**, *110*, 966.

impurities. (*E*) and (*Z*)-4-bromo-4-octene were prepared by literature methods.[13,14] Diethyl ether, THF, and benzene were distilled from sodium/benzophenone. 4-Octyne, CH_2Cl_2, hexane, and TMEDA were distilled from CaH_2.

Competition Experiments. A solution of the test substrate (3 equiv, 1.5 M), a standard (3 equiv, 1.5 M), an internal standard (mesitylene, 1 equiv), AIBN (0.12 equiv), tributyltin hydride (1 equiv, added last), and dry, degassed benzene was placed under an N_2, and the mixture was heated at 80 °C for 4 h. An aliquot was removed and diluted, and the yield of reduced products was measured by GC. Experiments conducted at ambient temperature were initiated by irradiation with an Ace-Hanovia 450-W high-pressure quartz mercury vapor lamp.

Calculation of Rate Constants. Absolute rate constants were calculated using an equation provided by Beckwith:[2b]

$$k_X = \frac{(k_Y) \log ([R^1X]/[R^1X]_o)}{\log ([R^2Y]/[R^2Y]_o)}$$

where k_X is the rate constant for atom (group) abstraction of the test substrate, k_Y is the rate constant for atom (group) abstraction of the standard, $[R^1X]$ and $[R^1X]_o$ are the final and initial concentrations of the test substrate, and $[R^2Y]$ and $[R^2Y]_o$ are the final and initial concentrations of the standard. The final concentrations were determined by subtracting the yields of reduced products from the starting concentrations.

Benzyl Chloroacetate. A solution of dry CH_2Cl_2 (55 mL), benzyl alcohol (4.5 mL, 43 mmol), and pyridine (3.5 mL, 43 mmol) was cooled to 0 °C with stirring, and chloroacetyl chloride (3.4 mL, 43 mmol) was slowly added dropwise. The reaction was then stirred at 25 °C for 15 min and then quenched in cold water. The two phases were separated, and the aqueous layer extracted twice with CH_2Cl_2. The organic extracts were combined and washed with water and then with brine. The CH_2Cl_2 solutions were dried over $MgSO_4$, filtered, and concentrated. The product was purified by vacuum distillation (bp 79–81 °C at 0.65 mmHg) to give 6.88 g (0.037 mol, 86%) of a colorless oil: ^1H NMR ($CDCl_3$) δ 7.35 (s, 5 H), 5,20 (s, 2 H), 4.08 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 134.93, 128.66, 128.46, 67.86, 40.89; IR (neat film) 1736, 1498, 1455, 1377, 1168, 749, 698 cm^{-1}; MS *m/e* 184, 108, 91, 77, 65, 51; HRMS for $C_9H_9ClO_2$ calcd 184.0291, found 184.0291.

Malonic Esters 12 and 13. NaH (12 mmol, 1.2 equiv) was suspended in dry THF at 0 °C, diethyl methylmalonate (10 mmol, 1.0 equiv) was added dropwise, and the reaction was stirred at 25 °C for 1 h. An alkylating agent (11 mmol, 1.1 equiv, 1,2-dibromo-2-propene for **12**, or 1,3-dibromo-1-propene for **13**) was added, and the reaction stirred at 25 °C for 7 h. The reaction was quenched in ice water and extracted several times with ether. Ether extracts were washed with water and then with brine. The ether solution was dried over $MgSO_4$, filtered, and concentrated. Products were purified by flash chromatography on silica in 8:1 hexane/ethyl acetate.

Diethyl (2-Bromo-1-prop-2-enyl)methylmalonate (12). The yield was 1.74 g (70%): ^1H NMR ($CDCl_3$) δ 5.6 (s, 1 H), 5.3 (t, J = 2 Hz, 1 H), 4.16 (q, J = 7 Hz, 4 H), 3.1 (d, J = 3 Hz, 2 H), 1.44 (s, 3 H), 1.21 (t, J = 7 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 171.3, 127.5, 121.7, 61.6, 53.1, 45.9, 19.3, 13.9; IR (neat film) 2940, 1731, 1625, 1448, 1266, 1297, 1206, 1023, 898, 860 cm^{-1}; MS *m/e* 247, 231, 219, 213, 201, 185, 175, 157, 139, 111, 67; HRMS for $C_{11}H_{17}O_4Br$ calcd 291.9970, found 246.9970 (M - OEt).

Diethyl (1-Bromo-3-prop-1-enyl)methylmalonate (13). The yield was 2.92 g (99%, mixture ~2/3 of cis and trans): ^1H NMR ($CDCl_3$) δ 6.25 (dd, J = 6, 1.5 Hz, 1 H, *Z*), *E*, 6.06 (m, 2 H, *E*; 1 H, *Z*), 4.14 (q, J = 7 Hz, 8 H), 2.72 (dd, J = 1 Hz, J = 1.6 Hz, 2 H, *E*), 2.51 (t, J = 3 Hz, 2 H, *Z*), 1.36 (s, 3 H, *E*), 1.33 (s, 3 H, *Z*), 1.19 (t, J = 7 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 171.6 (*E*), 171.4 (*Z*), 132.4 (*Z*), 129.4 (*E*), 111.1 (*E*), 108.6 (*Z*), 61.5 (*E* and *Z*), 53.2 (*Z*), 52.9 (*E*), 39.6 (*Z*), 35.8 (*E*), 19.9 (*E* and *Z*), 14.0 (*E* and *Z*); IR (neat film) 1737, 1622, 1449, 1366, 1334, 1296, 1023, 953, 860, 710, 664 cm^{-1}; MS *m/e* 292, 249, 213, 185, 139, 111, 69; HRMS for $C_{11}H_{17}O_4Br$ calcd 292.0310, found 292.0310.

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4-*tert*-Butyl-1-bromocyclohex-1-ene (14).[15] 4-*tert*-Butylcyclohexanone tosylhydrazone[16] (9.67 g, 30 mmol) was added to a three-neck flask and placed under N_2 atmosphere. Dry TMEDA (190 mL) was added via cannula, and the resulting suspension was cooled to −45 °C with vigorous stirring. A 1.6 M solution of *n*-butyllithium in hexanes (75 mL, 120 mmol) was added dropwise via an addition funnel, and the reaction was stirred at −45 °C for 30 min and then at 25 °C for 3 h. The reaction was cooled to 0 °C, and 1,2-dibromoethane (11 mL, 128 mmol) was added dropwise. The reaction was stirred at 25 °C for 1.5 h, quenched in 10% $NaHSO_4$(aq), and extracted several times with pentane. The pentane extracts were washed with 5% $NaHSO_4$(aq), water, saturated $CuSO_4$ (2×), and brine. The pentane solution was dried over $MgSO_4$, treated with decolorizing carbon, filtered through a pad of neutral alumina, and concentrated. The crude product was purified by vacuum distillation (bp 41–42 °C at 0.7 mmHg) to give 1.35 g (6.2 mmol, 21%) of a colorless oil: ^1H NMR ($CDCl_3$) δ 5.99 (t, J = 3 Hz, 1 H), 2.44 (q, J = 2 Hz, 2 H), 1.83 (dd, J = 3 Hz, 2 H), 1.31 (m, 2 H), 1.23 (m, 1 H), 0.84 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 128.9, 121.9, 42.9, 36.5, 32.2, 29.1, 27.2, 26.0; IR (neat film) 2901, 2842, 1655, 1478, 1434, 1394, 1046, 976, 906, 705 cm^{-1}; MS *m/e* 216, 201, 160, 137, 81, 69, 57; HRMS for $C_{10}H_{17}Br$ calcd 216.0514, found 216.0514.

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Registry No. 1, 3972-65-4; 2, 696-62-8; 3, 104-92-7; 4, 2398-37-0; 5, 578-57-4; 6, 99-90-1; 7, 2142-63-4; 8, 2142-69-0; 9, 623-00-7; 10, 6952-59-6; 11, 2042-37-7; 12, 137256-13-4; (*Z*)-13, 137256-14-5; (*E*)-13, 137256-15-6; 14, 23525-05-5; 15, 24291-80-3; 16, 24291-81-4; Bu_3SnH, 688-73-3; dimethyl methylmalonate, 609-08-5; 1,3-dibromo-1-propene, 627-15-6; 1,2-dibromo-2-propene, 513-31-5; 4-*tert*-butylcyclohexanone tosylhydrazone, 41780-53-4; benzyl chloroacetate, 140-18-1; 1-bromooctane, 111-83-1.

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Acidity of Imidodicarbonates and Tosylcarbamates in Dimethyl Sulfoxide. Correlation with Yields in the Mitsunobu Reaction

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Unsubstituted imidodicarbonates $R_1OCO-NH-COOR_2$, such as **1–13**, are useful phthalimide substitutes[1-3] in Gabriel[4] and Mitsunobu[5] reactions, and a tosylcarbamate **15** has also recently been applied to the latter context.[6] In connection with the synthesis of protected chiral alanine derivatives directly from lactate esters using the Mitsunobu reaction,[7] we noticed that some imidodicarbonates,[8] related to amino-protecting groups used in peptide synthesis,[9] reacted poorly, whereas others, probably more acidic ones, and, particularly, a few tosylcarbamates gave the expected products in much higher yields. To the best of our knowledge, no relevant acidity measurements of imidodicarbonates and tosylcarbamates have been reported in the literature so far. Therefore, the present investigation was undertaken with the goal of determining whether any correlation exists between the pK_a values of these NH acids and the yields[7] obtained in the Mitsunobu reactions.

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