Determination of Rate Constants for the Reaction of Aryl Radicals with Enolate Ions

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The rate of ring closure (k_C) of *o*-(ω-alkenyl)aryl radicals by means of an intramolecular attack of the intermediate phenyl-type radical at the tethered double bond was found to be 4.2×10^8 s^{-1} (for **1•**) and 7.6×10^7 s^{-1} (for **8•**), both being 6-*exo*-*trig* processes, and 9.6×10^9 s^{-1} for the 5-*exo*-*trig* process of **3•**. The k_C rate constant of these radicals was calibrated with respect to a known rate of H-atom abstraction (k_H). The photostimulated $S_{RN}1$ reactions of radical clock precursor **1** with anions PhS^- and $(EtO)_2PO^-$ in Me_2SO at 25 °C provided the rates of addition of these nucleophiles (k_Y) to intermediate **1•** (3.2×10^8 and 2.5×10^9 M^{-1} s^{-1}, respectively). In contrast, the analogous reaction of a ketone enolate ion with precursor **1** did not take the expected $S_{RN}1$ course; instead an elimination reaction was favoured. Similarly, the reactions of radical clock precursors **3** or **8** with the enolate ion failed. However, investigation of the distribution of 9-anthracenyl (**11•**) or 1-naphthyl (**12•**) radicals between two competing reactions, namely combination with a nucleophile and H abstraction from the solvent (Me_2SO), was successful and eventually enabled us to find the k_Y values for the addition of the enolate ion to these two aryl radical intermediates (4.4×10^8 and 2.9×10^9 M^{-1} s^{-1}, respectively).

Introduction

Aromatic nucleophilic substitutions proceeding by free-radical chains (the $S_{RN}1$ mechanism, Scheme 1) have been the subject of intense scrutiny in the last two decades.[1]

$$ArX \xrightarrow{e^-} ArX^{\bullet -}$$

$$ArX^{\bullet -} \rightarrow Ar^{\bullet} + X^-$$

$$Ar^{\bullet} + Y^- \rightarrow ArY^{\bullet -}$$

$$ArY^{\bullet -} + ArX \rightarrow ArY + ArX^{\bullet -}$$

Scheme 1

Activation of the substrate (typically an aryl halide ArX) by electron transfer causes the fragmentation of the bond between the carbon atom and the leaving group, thereby enabling subsequent attack by a nucleophile (Y^-) at the intermediate aryl radical (an associative electron-transfer process).[1,2] This results in the formation of the substitution product, through the fleeting intermediacy of its radical anion,[2b] and in the propagation of the chain process.

The preliminary conversion of precursor ArX into a radical anion weakens the C−X bond: the extent of this weakening effect has been assessed,[3] and rate constants for the cleavage of the C−X bond in several $ArX^{\bullet -}$ have been obtained.[4] Instead, only a few kinetic data are available for the subsequent addition of nucleophiles to the aryl radical intermediate. By an electrochemical approach,[5] the group of Savéant was able to measure the rate of addition of PhS^-, $CH_3COCH_2^-$ and $(EtO)_2PO^-$ ions to $Ph^{\bullet}$ in NH_3 at −33 °C. The measured rates were 2.6×10^7, 2.7×10^8, and 3.8×10^8 M^{-1} s^{-1}, respectively. Rate constants for the addition of the same nucleophiles to the 1-naphthyl radical were higher, and very close to the diffusion limit.[6] By making use of a radical clock,[7] Beckwith and Palacios obtained a value of 2.6×10^8 M^{-1} s^{-1} for the rate of addition of PhS^- to an *ortho*-(alkenyloxy)phenyl radical in Me_2SO at 25 °C, but were unable to measure the rate of addition of the enolate of pinacolone to the same radical. This failure appeared puzzling to us, since the enolate ions are the most well-behaved nucleophiles in $S_{RN}1$ processes,[1b] and the thermodynamic driving force for their addition to the phenyl radical have been shown by calculations to be very favourable.[8] Therefore, the lack of reactivity of an enolate ion with the above *ortho*-(alkenyloxy)phenyl radical[7] arose our curiosity, and prompted this investigation. As the radical clock approach[9] also failed in our hands, we resorted to other competition experiments in order to achieve our goal.

Results and Discussion

Calibration of the Method

Beckwith and Palacios employed *o*-(but-3-enyloxy)iodobenzene (**1**) as the radical clock precursor in the photostimulated $S_{RN}1$ reactions with a few nucleophiles,[7] according to the reaction scheme outlined below (Scheme 2).[1,2e]

The crucial intermediate **1•** may, in principle, be distributed along three pathways: (i) abstraction of a hydrogen atom from the medium (k_H), leading to hydrodeiodinated product **1H**; (ii) intramolecular attack (k_C) at the tethered double bond, affording the exocyclic radical **2•** in a 6-*exo*-*trig* process;[10] (iii) reaction with the nucleophile (k_Y, the

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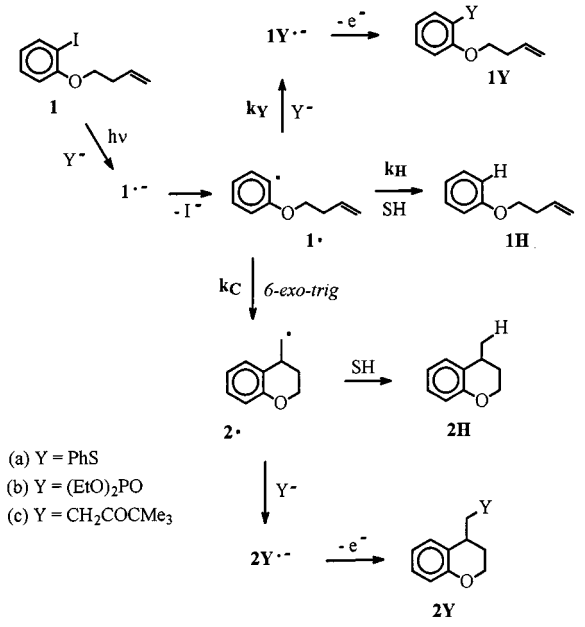


Scheme 2

$S_{RN}1$ process), leading to radical anion **1Y•⁻**. If the rate constant k_C is known, the k_Y value can be calculated.[7] Preliminarily, k_C is obtained by calibration against a suitable H-atom donor whose k_H rate is known.[9] A recent reevaluation of the k_H value for the deprotonation of Bu_3SnH by a phenyl radical in benzene at 25 °C (i.e. 7.8×10^8 M^{-1} s^{-1})[11] prompted us to calibrate the k_C of **1•** once again, and a value of 4.2×10^8 s^{-1} was obtained (Table 1). This value of k_C correlates well with that previously obtained by using the same method (1.3×10^8 s^{-1}),[7] when the previous k_H value (6.4×10^8 M^{-1} s^{-1}) was used.[7] All rate constants were measured at 25 °C.

The photostimulated $S_{RN}1$ reaction of PhS^- with **1** in Me_2SO was then repeated,[7] and we could derive $k_Y = 3.2 \times 10^8$ M^{-1} s^{-1} for the addition of PhS^- to **1•** at 25 °C (Table 2). This value is ten times higher than that determined electrochemically at a much lower temperature (−33 °C in liquid ammonia),[5] and is in good agreement with the value previously determined by the same approach (2.6×10^8 M^{-1} s^{-1}).[7]

Reactions of Phenyl-Type Radical Clocks with Nucleophiles

The photostimulated reaction of **1** with $(EtO)_2PO^-$ in Me_2SO was then carried out using the same approach (Scheme 2).[7] The value of k_Y for the reaction with **1•** was found to be 2.5×10^9 M^{-1} s^{-1} at 25 °C. This value is 6 times higher than that obtained in liquid ammonia.[5,7] More importantly, it confirms that $(EtO)_2PO^-$ is more reactive than PhS^- in aromatic $S_{RN}1$ reactions.[12] The higher reactivity can be rationalized thermodynamically: the energy of the C−P bond (112 kcal/mol) formed in the substitution product **1Yb** is greater than the C−S bond energy (81 kcal/mol) of **1Ya**.[8] Also, the intermediate radical anion **1Yb•⁻** ($E° = -2.57$ V) is more stable than **1Ya•⁻** ($E^p \geq -2.7$ V). Therefore, there is a higher thermodynamic driving force for addition of the phosphorus than of the sulfur nucleophile to the phenyl radical,[8] and this parallels the corresponding kinetic efficiency (k_C).

Table 1. Determination of k_C rate constants (at 25 °C) for the radical clock employed; under photolysis at 350 nm for 0.5−2 h

Radical	Precursor (mmol)	Conditions	H donor (mmol)	Cyclic product (mmol)	ArH (mmol)	k_C (s^{-1})[a]
1•	**1** (0.90)	in 1.8 mL of benzene with 0.09 mmol of AIBN	Bu_3SnH (0.80)	**2H** (0.24)	**1H** (0.18)	4.2×10^8
3•	**3** (0.23)	in 1.75 mL of Me_2SO [b] with 0.03 mmol of AIBN	PhSH (0.74)	**4H** (0.17)	**3H** (0.012)	9.6×10^9
6•	**6** (0.24)	in 1.75 mL of Me_2SO [b] with 0.03 mmol of AIBN	PhSH (0.70)	**7H** (0.19)	**6H** (0.010)	1.2×10^{10}
8•	**8** (0.053)	in 2.4 mL of benzene	Bu_3SnH (0.42)	**9H** (0.015)	**8H** (0.026)	7.6×10^7

[a] From the relationship: k_C/k_H = ([cyclic prod.] × [H donor])/[ArH]; where $k_H = 7.8\times10^8$ M^{-1}s^{-1} for Bu_3SnH or 1.9×10^9 M^{-1}s^{-1} for PhSH, both data at 25 °C. Experiments were duplicated, and the tabulated molar amounts are the averages of several GC injections; propagation of the errors gives an accuracy of ≤ 10% to the rate constants. − [b] Containing 0.26 mL of Bu_3SnH to minimize disulfide formation.

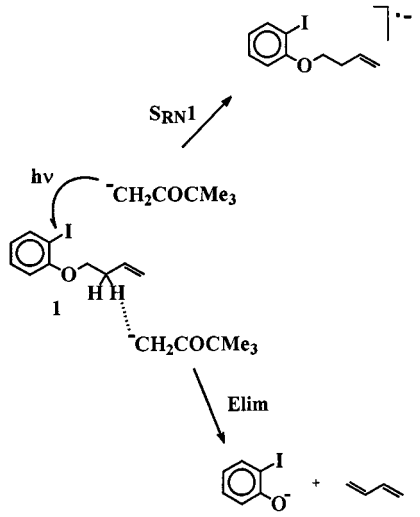
Table 2. Summary of the k_Y rate constants determined in Me_2SO at 25 °C; under photostimulation at 350 nm for 20−60 min

Radical	Precursor (mmol)	Conditions	Y^- (mmol)	Subst. prod. (mmol)	Reduct. prod. (mmol)	Other (mmol)	Rate const.[a] (M^{-1} s^{-1})
1•	**1** (0.2)	in 5 mL of Me_2SO and 0.82 mmol of *t*BuOK	PhS^- (0.78)	**1Ya** (0.010)	**2H** (0.076)	**2Ya** (0.008)	$k_Y = 3.2\times10^8$
1•	**1** (0.1)	in 5 mL of Me_2SO and 0.32 mmol of *t*BuOK	$(EtO)_2PO^-$ (0.28)	**1Yb** (0.019)	**2H** (0.052)	**2Yb** (0.005)	$k_Y = 2.5\times10^9$
11•	**11** (0.2)	in 4 mL of Me_2SO and 0.33 mmol of *t*BuOK	$Me_3CCOCH_2^-$ (0.29)	**11Y** (0.049)	**11H** (0.013)	−	$k_Y = 4.4\times10^8$
12•	**12** (0.1)	in 3 mL of Me_2SO and 0.33 mmol of *t*BuOK	$Me_3CCOCH_2^-$ (0.29)	**12Y** (0.062)	**12H** (0.022)	−	$k_Y = 2.9\times10^9$

[a] From duplicated experiments: average error ≤ 10%.

We also attempted photostimulated reactions of **1** with either NO_2^- or CN^- as nucleophiles, but no substitution products were obtained. Instead, some photohomolysis of the C−I bond of **1** was observed,[13] with ensuing production of minor amounts of reduction products **1H** and **2H**. The lack of reactivity of NO_2^- or CN^-, in spite of a favourable thermodynamic driving force for their associative electron transfer to the phenyl radical, has already been mentioned.[8] The positive oxidation potential of these ions is a possible reason for the lack of kinetic efficiency in $S_{RN}1$ reactions.[8]

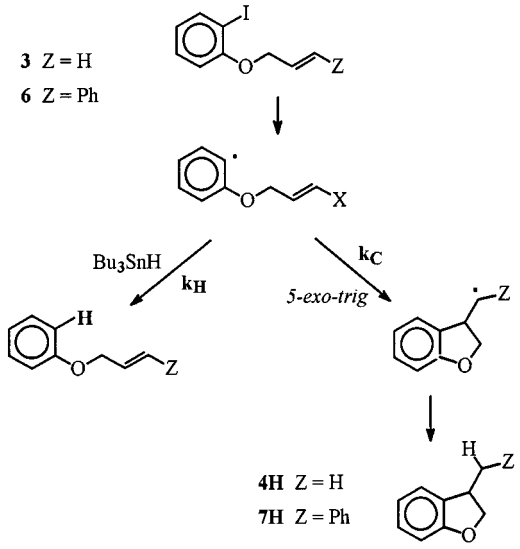
In spite of the ample literature reports of efficient $S_{RN}1$ reactions with ketone enolate ions,[1] **1** was reported to have failed to react with the enolate of pinacolone in Me_2SO under photostimulation.[7] By repeating this experiment, we confirmed the lack of formation of substitution product **1Yc** (Scheme 2). However, precursor **1** was consumed, and sizeable amounts of *o*-iodophenol could be recovered from the water phase during workup. An elimination process could then be envisioned in which the enolate ion acts as a base rather than as a reductant, as would instead be required for the photoinduced electron transfer to the substrate (Scheme 3).[2e]



Scheme 3

The enolate ion is indeed a stronger base[14] than the two nucleophiles favourably tested here [PhS^- and $(EtO)_2PO^-$]. The elimination of the allylic hydrogen atoms of **1** would then become possible, and be made easier by the formation of 1,3-butadiene as a neutral leaving fragment, along with the loss of the good leaving group, *o*-iodophenoxide. In this case, the elimination process would cleave precursor **1** and prevent it from playing the role of a radical clock, thus explaining the failure of the expected $S_{RN}1$ reaction.[7] No effort was made to trap and detect gaseous butadiene. The reaction was instead modified by replacing pinacolone by acetophenone in the hope of suppressing the elimination reaction; the enolate of the latter is a thousand times weaker as a base than the enolate of pinacolone.[14a] No major difference could be recorded.

It appeared worthwhile to develop a modified radical clock whose structure precluded the elimination process that was suggested to take place with **1**. Precursor **3** was synthesised: its *O*-allyl chain ought to prevent the elimination step delineated in Scheme 4. Precursor **3** was calibrated, giving a k_C value of 9.6×10^9 s^{-1} at 25 °C (Table 1 and Scheme 4). This is a 5-*exo-trig* process, which is indeed expected to be faster than the 6-*exo-trig* process of **1**.[10,15]

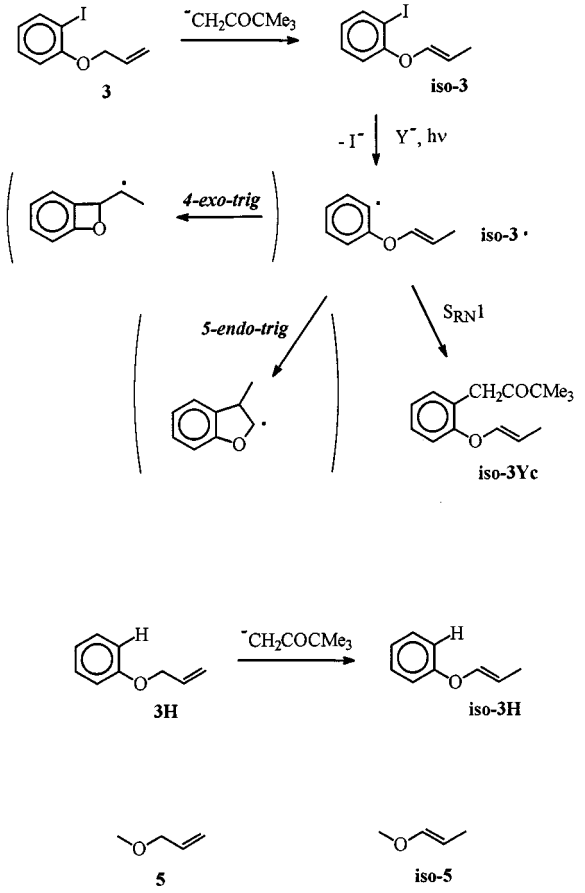


Scheme 4

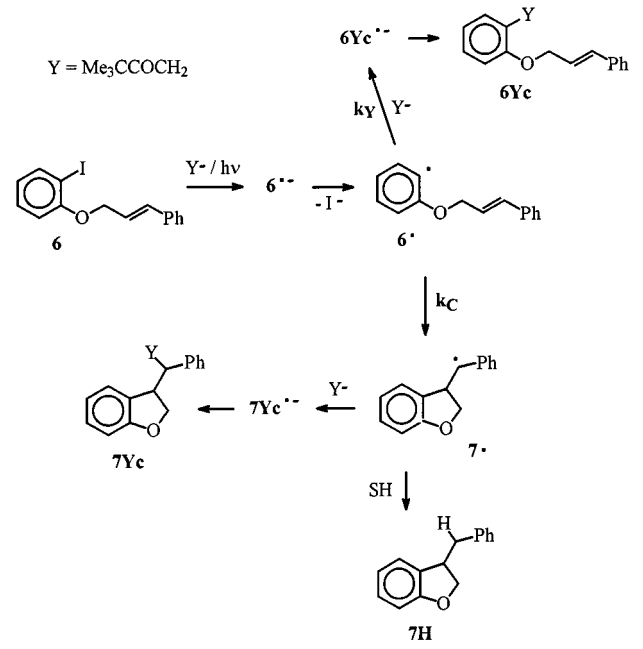
Unfortunately, when the photostimulated $S_{RN}1$ reaction of **3** with $Me_3CCOCH_2^-$ was attempted in Me_2SO, another unexpected process prevented our attempt to measure the k_Y value. Although an $S_{RN}1$ product was obtained, careful analysis of its NMR spectrum revealed that the *O*-allyl ether moiety in the side-chain had isomerised to a 1-propenyl ether. Had any base-induced isomerisation of **3** (to **iso-3**) *preceded* the photoinduced electron transfer to the substrate, then the radical clock approach would fail (Scheme 5). In fact, any **iso-3•** intermediate would be unable to rearrange intramolecularly, since those pathways are either 5-*endo-trig* or 4-*exo-trig* processes and both are expected to be highly unfavourable.[10] Therefore, there would be no intramolecular process to compete with the intermolecular $S_{RN}1$ reaction leading from **iso-3•** to **iso-3Yc**.

In order to verify this hypothesis, **3H** was exposed to the enolate ion, and fast isomerisation to **iso-3H** did occur. Such an isomerisation is thermochemically favoured: semiempirical calculations of the heat of formation of model structures **5** and **iso-5** showed that **iso-5** is more stable than **5** by 6 kcal/mol. Therefore, a fast base-induced isomerisation of radical clock **3** to **iso-3** is likely to occur: it would anticipate any expected electron-transfer evolution of **3**. The $S_{RN}1$ process would then take place at **iso-3**.

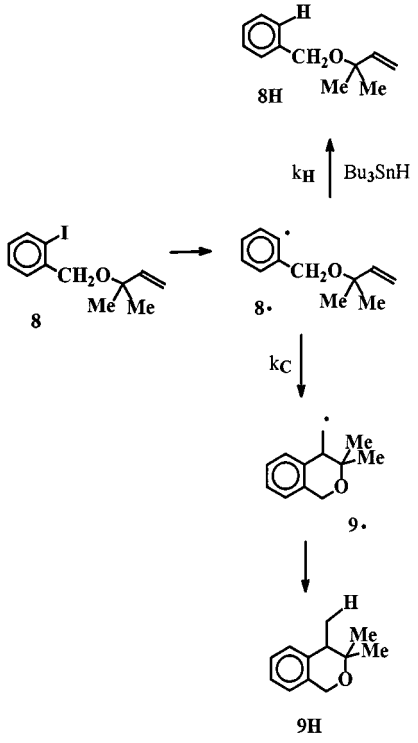
In the hope that the appropriate stabilisation of the allylic side-chain of **3** would prevent the above base-induced isomerisation, precursor **6** was sought. It features an *O*-cinnamyl chain, in which the conjugate interaction of the styryl moiety would be likely to impede the isomerisation into a vinyl ether. Radical clock **6** was synthesised and calibrated



Scheme 5



Scheme 6



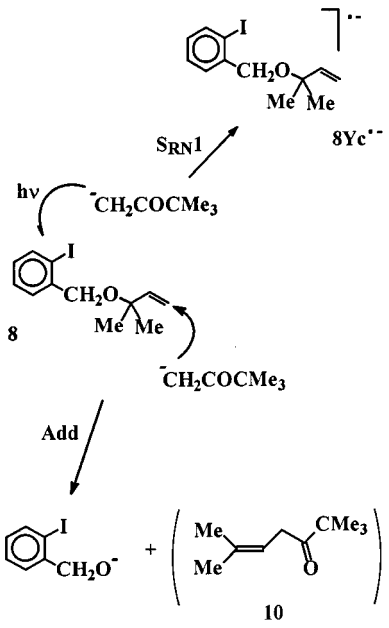
Scheme 7

as for **3** (Scheme 4), providing a k_C value of 1.2×10^{10} s^{-1} at 25 °C (Table 1). This made it the fastest ring closure found in this work. This was instrumental in our subsequent failure. In fact, while no appreciable interference from base isomerisation of **6** to **iso-6** occurred with the enolate of pinacolone (as had been hoped), the extremely fast 5-*exo-trig* ring closure of intermediate **6•** did prevent any appreciable competition from the intermolecular attack of the nucleophile. No traces of **6Yc** could be detected, and therefore k_Y could not be determined. Only products **7Yc** and **7H** were obtained (Scheme 6), both being derived from processes subsequent to the rapid **6•** → **7•** rearrangement.

We therefore searched for another radical clock, whose structure could preclude any base-promoted competing reaction, and whose k_C was not fast enough to override competition from the k_Y of the enolate ion. Precursor **8** appeared to possess the required features, in that the *gem*-dimethyl group could prevent any base-induced isomerisation, and radical intermediate **8•** ought to give a "slower" 6-*exo-trig* process.[10] Synthesis and calibration of **8** (Scheme 7 and Table 1) gave $k_C = 7.6 \times 10^7$ s^{-1} at 25 °C.

Even clock **8**, however, frustrated our attempts to obtain the k_Y value for the enolate ion. In fact, substantial amounts of *o*-iodobenzyl alcohol were detected by GC-MS after workup; it is reasonable to infer that the enolate ion behaved as a nucleophile in an ionic addition to the double bond of **8**, causing the elimination of *o*-iodobenzylalkoxide (Scheme 8) and preventing the occurrence of the $S_{RN}1$ process.

No traces of oxoalkene **10**, likely to result from this addition step, were detected. Perhaps, condensation and/or oligomerisation processes of **10** occurred under the experimental conditions. In view of the absence of the desired $S_{RN}1$ evolution of precursor **8**, the suggested addition process of Scheme 8 was not further investigated, use of the radical clocks was dismissed, and another competition

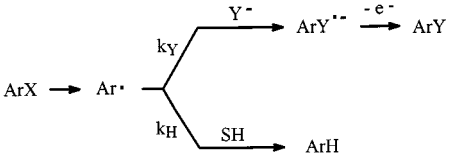


Scheme 8

method for the determination of k_Y for the enolate ion was devised.

Competition Between Substitution and H-Atom Abstraction

The $S_{RN}1$ mechanism (Scheme 1) allows for the intermediate aryl radical to undergo either a combination with the nucleophile or an H-atom abstraction from the solvent (or another species).[16] In general, the latter process cannot be quantified by product analysis for simple phenyl halides, whose reduced product (i.e. benzene) prevents GC detection in view of its low boiling point. However, reduced products with higher boiling points can be detected precisely, and if the specific H-atom abstraction process (k_H) is known, the competing k_Y of the nucleophile can be evaluated (Scheme 9).



Y• = $^-CH_2COCMe_3$ **11** Ar = 9-Anthr

SH = Me_2SO **12** Ar = 1-Naphth

$k_Y/k_H = [ArY][SH] / [ArH][Y^-]$

Scheme 9. X = Br

This scheme was tested for 9-bromoanthracene (**11**) and 1-bromonaphthalene (**12**). In fact, the rate constants of H abstraction from Me_2SO by the intermediate 9-anthracenyl radical (**11•**; $k_H = 6.0 \times 10^5$ M^{-1} s^{-1}) and the 1-naphthyl radical (**12•**; $k_H = 7.1 \times 10^6$ M^{-1} s^{-1}),[16,17] were available. When the photostimulated reactions of these substrates with the pinacolone enolate ion were performed in Me_2SO at 25 °C, both the substitution and reduced products were detected, and k_Y could be calculated. For **11•** we obtained $k_Y = 4.4 \times 10^8$ M^{-1} s^{-1}, and for **12•**, $k_Y = 2.9 \times 10^9$ M^{-1} s^{-1} (Table 2). Both rate constants are rather high, as expected for an efficient addition of the enolate ion.[1,8,12] Unfortunately, only an approximate k_H value (ca. 1×10^6 M^{-1} s^{-1})[16] is presently available for H abstraction from Me_2SO in the case of the phenyl radical itself, thus precluding an experiment such as that shown in Scheme 9. We are, indeed, trying to obtain a more reliable value of k_H for the reaction of the phenyl radical with Me_2SO. If this becomes available, we could run a photostimulated reaction of $Me_3CCOCH_2^-$ with an appropriate phenyl radical precursor (i.e., one whose reduced product can be detected by GC) in Me_2SO, as reported above for **11•** and **12•**, and hopefully determine the desired k_Y value.

Experimental Section

General Remarks: Photochemical reactions were conducted in a Rayonet RPR-100 reactor equipped with a set of 16 350-nm lamps (Pyrex-filtered). Temperature control is critical for accurate rate-constant determinations, and therefore a water-jacketed glass flask (10 mL capacity) under thermostat control was employed in the photostimulated experiments, so as to prevent the heat of the lamps from increasing the temperature of the reacting solution during irradiation. The dimensions of the water-jacketed flask fitted in the hole of the RPR-100 reactor, and a connection to an external thermostat by appropriate tubes was made. Semiempirical calculations were carried out by using the HyperChem package.[18] The reaction products were characterised by NMR spectroscopy at 200 and at 300 MHz with Bruker instruments, and by GC-MS with an HP 5972 MSD at 70 eV. Chemical shifts are reported in ppm (δ scale) relative to residual non-deuterated solvent signals ($CDCl_3$). GC-MS and GC analyses were run on methylsilicone capillary columns. Commercial chemicals (Aldrich) were used without further purification. Benzene was dried with sodium wire, while Me_2SO was distilled from CaH_2 and stored over activated molecular sieves (4 Å). The conjugate acids of the anions were distilled prior to use; freshly sublimed potassium *tert*-butoxide was used to generate the anions in the photostimulated experiments in Me_2SO. KNO_2 and KCN (C. ERBA RPE) were used as received.

Synthesis of Precursors: 9-Bromoanthracene (**11**) and 1-bromonaphthalene (**12**) were commercial samples. Precursor **1** was synthesised from *o*-iodophenoxide and 4-bromo-1-butene as described.[7] It can be seen that a base-induced eliminative cleavage of **1** (in keeping with Scheme 3) occurred to a minor extent owing to the slight excess of KOH employed to generate the phenoxide ion. Precursors **3** and **6** were also obtained from *o*-iodophenoxide and allyl or cinammyl bromide, respectively.[19] – Compound **8** was obtained in a two-step synthesis, starting from side-chain chlorination of *o*-iodobenzyl alcohol (1.03 g, 4.4 mmol; Aldrich) with Ph_3P (1.2 g, 4.5 mmol) in refluxing CCl_4 (15 mL) for 24 h.[20] *o*-Iodobenzyl chloride (1.0 g, 87%) was obtained as a white solid with a low melting point (*m/z*: 252 and 254 [M^+]). The latter was directly employed in the subsequent reaction with commercial 2-methyl-3-buten-2-ol (7 mmol) and NaH (7.5 mmol) in refluxing THF (15 mL) for 36 h. After conventional workup, the crude **8** was distilled, bp 95–100 °C at 30 Torr (0.5 g; 44% yield). – ^1H NMR ($CDCl_3$): δ = 7.8–6.9 (m, 4 H, ArH), 5.9 (dd, 1 H, CH=), 5.2 (m,

2 H, CH_2=), 4.3 (s, 2 H, $ArCH_2$), 1.4 (s, 6 H, Me). − ^{13}C NMR ($CDCl_3$): δ = 143 (*C*H=), 141−128 (aromatic carbon atoms), 114 (*C*H_2=), 97 (C^{Ar}_{ipso}−I), 77.5 (C^{tert}−O), 76 (Ar*C*H_2O), 26 (Me). − MS; *m*/*z*: 302 [M^+], 287 [M^+ − Me], 217 [M^+ − $OCMe_2CH$=CH_2]. − $C_{12}H_{15}IO$ (302.15): calcd. C 47.68, H 4.97; found C 47.99, H 4.78.

Synthesis of Products: Anthracene (**11H**), and naphthalene (**12H**) were commercial samples. Analytical samples of **1H**, **3H**, and **6H** were prepared by alkylation of phenoxide ion with either 4-bromo-1-butene, allyl bromide or cinammyl bromide, respectively; product **8H** was obtained from the alkylation of benzyl bromide with sodium 2-methyl-3-butenyl-2-oxide (see above). All these products were purified by flash chromatography, characterised by MS, and used for the determination of the GC response factor. In the case of **9H**, the response factor of isomeric **8H** was employed. Products **1Ya**, **1Yb**, **2Ya**, **2Yb** were obtained from $S_{RN}1$ photochemical experiments (vide infra), run on a larger scale in a normal flask without temperature control during irradiation, and purified by chromatography. Their NMR features were consistent with those already reported.[7] During chromatography of the residues of these reactions, product **2H** was also obtained in small amounts, as a forerun fraction. − **2H** (oil): ^{1}H NMR ($CDCl_3$): δ = 7.0−6.7 (m, 4 H, ArH), 4.00−3.95 (br. t, 2 H, OCH_2), 2.99−2.92 (m, 1 H, ArCH), 1.69−1.63 (m, 2 H, CH_2), 1.20−1.15 (dt, 3 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 156 (C^{Ar}_{ipso}−O), 131−128 (aromatic carbon atoms), 117 (C^{Ar}_{ipso}−CH), 69 (O*C*H_2), 32 (*C*H_2), 30 (Ar*C*H), 18 (*C*H_3). − Analytical samples of **4H** and **7H** were obtained from the hydrodeiodination of **3** or **6** with Bu_3SnH in boiling benzene. − **4H** (oil): ^{1}H NMR ($CDCl_3$): δ = 7.0−6.8 (m, 4 H, ArH), 4.50−4.35 (d, 2 H, OCH_2), 3.30−3.15 (m, 1 H, ArCH), 1.18−1.15 (d, 3 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 154 (C^{Ar}_{ipso}−O), 130−128 (aromatic carbon atoms), 118 (C^{Ar}_{ipso}−CH), 73 (O*C*H_2), 31 (Ar*C*H), 16 (*C*H_3). − **7H** (oil): ^{1}H NMR ($CDCl_3$): δ = 7.3−6.8 (m, 9 H, ArH), 4.45−4.30 (dt, 2 H, OCH_2), 3.75−3.60 (m, 1 H, ArCH), 3.10−2.85 (m, 2 H, $PhCH_2$). − ^{13}C NMR ($CDCl_3$): δ = 158 (C^{Ar}_{ipso}−O), 131−126 (aromatic carbon atoms), 140 (C^{Ph}_{ipso}−CH_2), 120 (C^{Ar}_{ipso}−CH), 75 (*C*H_2), 40 (Ar*C*H), 37 (Ph*C*H_2). − Products **11Y** and **12Y** were available from a previous investigation.[12b] − Product **7Yc** was obtained from the photostimulated reaction (350 nm) of **6** (0.13 g, 0.6 mmol) with Me_3CCOCH_3 (240 μL, 1.9 mmol) and *t*BuOK (0.23 g, 2.0 mmol) in Me_2SO (8 mL) for 2 h. Workup with brine and diethyl ether, followed by chromatography with hexane/$CHCl_3$ (9:1) on silica gel, gave **7Yc** as an oil (70 mg, 38%). − ^{1}H NMR ($CDCl_3$): δ = 7.6−6.7 (m, 9 H, ArH), 4.65 (dt, 2 H, $ArOCH_2$), 3.75 (dq, 1 H, ArCH), 3.45 (dq, 1 H, CH_2CHPh), 3.0−2.7 (m, 2 H, CH_2CO), 1.1 (s, 9 H, C*Me*$_3$). − ^{13}C NMR ($CDCl_3$): δ = 212 (*C*=O), 138−115 (aromatic carbon atoms), 74 ($ArOCH_2$), 43 (*C*Me_3), 41 (*C*H_2CO) 38 (Ar*C*H), 34 (CH_2CHPh), 23 (C*Me*$_3$). − Compound **iso-3Yc** was obtained from the photostimulated reaction (350 nm) of **3** (0.37 g, 1.4 mmol) with Me_3CCOCH_3 (0.8 mL, 6.4 mmol) and *t*BuOK (0.73 g, 6.5 mmol) in Me_2SO (20 mL) for 2 h. After workup with diethyl ether, column chromatography of the residue with hexane/$CHCl_3$ (9:1) on silica gel gave an oil (0.23 g, 71%), whose NMR spectra are consistent with the structure of **iso-3Yc**. − ^{1}H NMR ($CDCl_3$): δ = 7.3−6.8 (m, 4 H, ArH), 6.3 (dd, 1 H, OCH=), 4.8 (quint, 1 H, MeC*H*=), 3.8 (s, 2 H, $ArCH_2CO$), 1.6 (dd, 3 H, C*H*$_3$CH=), 1.2 (s, 9 H, C*Me*$_3$). − ^{13}C NMR ($CDCl_3$): δ = 213 (*C*=O), 142 (O*C*H=), 115 (Me*C*H=), 45 (*C*Me_3), 36 (Ar*C*H_2CO), 27 (C*Me*$_3$), 9 (*C*H_3CH=). − A DEPT experiment confirmed the presence of *only one* methylene group: δ = 36 (Ar*C*H_2CO). − MS; *m*/*z*: 232 [M^+], 191 [M^+ − CH=CHMe], 175 [M^+ − OCH=CHMe], 147 [M^+ − $COCMe_3$], 85 [$COCMe_3$], 57 [CMe_3].

General Procedure of Calibration of a Radical Clock: Precursor **1** (0.9 mmol) was irradiated at 350 nm in benzene (1.8 mL) in the presence of Bu_3SnH (0.8 mmol) and azobis(isobutyronitrile) (AIBN; 0.09 mmol) for 60 min.[13] The reaction flask was kept at 25 °C by means of its glass jacket connected to an external thermostat. At the end, an internal standard was added (biphenyl), and direct analysis of the sample (no workup) by GC and GC-MS gave the molar amount of the open-chain reduction product **1H**, along with that of the cyclised reduction product **2H**. By using the relationship k_C/k_H = ([**2H**] × [Bu_3SnH])/[**1H**], we were able to calculate the value of k_C, since the amount of tin hydride present and the value of k_H are known. In the case of precursor **3** (and **6**), the rapid ring closure of the intermediate open-chain radical to the ring-closed radical prevented the formation of any open-chain reduced product **3H** (and **6H**), even when run with a larger amount of Bu_3SnH. A more efficient H-atom donor was sought and found in PhSH, whose k_H rate constant in the reaction with the phenyl radical is 1.9×10^9 M^{-1} s^{-1} at 25 °C.[21] Therefore, the calibration of clocks **3** and **6** (0.23 mmol each) was conducted as for **1**, but employing PhSH (0.70 mmol) and AIBN (0.03 mmol) in Me_2SO (1.75 mL) and Bu_3SnH (0.26 mL). The values of k_C could thus be calculated.

General Procedure for Photostimulated $S_{RN}1$ Reaction: Under a stream of argon, the radical clock precursor (0.2 mmol) was added to a solution of the precursor of the anion (0.7 mmol) and *t*BuOK (0.8 mmol) in Me_2SO (5 mL). The mixture was stirred at 25 °C under argon while irradiated with 16 "350-nm" lamps. After an appropriate time, typically 20−60 min, the irradiation was stopped, brine and crushed ice were added, together with a suitable amount of an internal standard (biphenyl), and the mixture was worked up with diethyl ether. Concentration to a small volume, and analyses by GC and GC-MS, allowed for the measurement of the molar amount of the products formed and for the calculation of k_Y according to the relationship k_Y/k_C = [**1Y**]/([**2H**] + [**2Y**])[Y^-]. The photostimulated reactions of **11** or **12** (0.2 mmol) with Me_3C-$COCH_3$ (0.29 mmol) and *t*BuOK (0.33 mmol) in Me_2SO (4 mL) were run analogously for ca. 20 min. Analyses as above gave the molar amounts of the substitution and reduction products, from which k_Y could be reckoned according to the relationship: [ArY]/[ArH] = k_Y [Y^-]/k_H[SH], using 14.1 M for the concentration of neat Me_2SO.

Base-Catalysed Isomerisation of 3H: This reaction was conducted at room temperature in Me_2SO with an equimolar amount of $Me_3CCOCH_2^-$ K^+. Workup with diethyl ether and evaporation of the solvent left a residue that was carefully distilled in order to remove Me_3CCOCH_3 (bp. 100 °C). The residue consisted mainly of **iso-3H**, contaminated with ca. 20% of **3H**. Similar isomerisations of allyl ethers to 1-propenyl ethers have been reported.[22] − **3H**: ^{1}H NMR ($CDCl_3$): δ = 7.3−6.9 (m, 5 H, ArH), 6.2−6.0 (m, 1 H, CH=), 5.50−5.25 (br. q, 2 H, CH_2=), 4.55 (dd, 2 H, OCH_2). − ^{13}C NMR ($CDCl_3$): δ = 158 (C^{Ar}_{ipso} −O), 130 (*C*H_2=), 116 (CH=), 69 (O*C*H_2). − **iso-3H**: ^{1}H NMR ($CDCl_3$): δ = 7.3−6.8 (m, 5 H, ArH), 6.35 (dd, 1 H, OCH=), 4.8 (m, 1 H, =CHMe), 1.7 (dd, 3 H, Me). − ^{13}C NMR ($CDCl_3$): δ = 158 (C^{Ar}_{ipso} −O), 141 (O*C*H=), 107 (=*C*HMe), 26 (Me).

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