4.56. Found: C, 50.83; H, 3.05; N, 4.31.) **9** (190 mg, 29%): oil; ^1H NMR ($CDCl_3$) δ 3.57 (s, 3 H), 6.39 (d, J = 4 Hz, 1 H), 7.14 (d, J = 4 Hz, 1 H), 7.45–7.53 (m, 3 H), 7.73–7.77 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 51.9, 109.4, 114.9, 123.8, 126.3, 128.9, 129.8, 132.5, 133.8, 160.0, 167.1; MS, m/z (relative intensity) 309 (35), 307 (36), 278 (3), 276 (3), 251 (3), 249 (3), 230 (100); precise mass calcd for $C_{13}H_{10}BrNO_3$ 306.9845, found 306.9840.

Reaction of *N*-Benzoyl-(2*R*,*S*)-alanine Methyl Ester (2a) with DTBP. A mixture of *N*-benzoyl-(2*R*,*S*)-alanine methyl ester (**2a**) (0.3 g, 1.5 mmol) and DTBP (4 mL, 19 mmol) in *tert*-butyl alcohol (30 mL), contained in a quartz tube under nitrogen, was irradiated in the Rayonet photochemical reactor. After 4 days the reaction mixture was concentrated and chromatographed on silica with ethyl acetate–hexane as eluent to give dimethyl 2,3-dibenzamido-2,3-dimethylbutanedioate (**13**) and *N*-benzoyl-2,2-dimethylglycine methyl ester (**12**). **13** (60 mg, 20%): mp 170–177 °C; ^1H NMR (DMSO-d_6) δ 2.00 (s, 6 H), 3.80 (s, 6 H), 6.80 (br, 2 H), 7.53–7.93 (m, 10 H); MS, m/z (relative intensity) 413 (0.4), 381 (2), 353 (7), 231 (22), 207 (38), 175 (8), 105 (100), 77 (50). (Anal. Calcd for $C_{22}H_{24}N_2O_6$: C, 64.1; H, 5.9; N, 6.8. Found: C, 63.9; H, 5.9; N, 6.6.) **12** (32 mg, 10%) was identical in all respects with an authentic sample obtained by derivatization of the corresponding amino acid.[36]

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Registry No. 1a, 1205-08-9; **1b**, 102770-12-7; (2*S*)-**2a**, 38767-73-6; (2*R*)-**2a**, 7260-27-7; (2*RS*)-**2a**, 38767-73-6; (2*S*)-**2b**, 118013-54-0; (2*R*)-**3a**, 1492-13-3; (2*RS*)-**3a**, 14599-03-2; (2*S*)-**3b**, 116297-93-9; **4a**, 71533-21-6; (2*RS*)-**5a**, 54571-66-3; (2*RS*)-**5b**, 117918-31-7; (2*RS*)-**6a**, 114051-14-8; (2*RS*)-**6b**, 117918-32-8; (2*RS*)-**6c**, 117918-33-9; **9**, 117918-26-0; **10**, 117918-27-1; **11**, 117918-28-2; **12**, 65563-98-6; (±)-**13** (diastereomer-1), 117918-29-3; (±)-**13** (diastereomer-2), 117918-34-0; **14**, 117918-30-6; **15**, 116453-15-7.

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Steric and Electrochemical Effects on Rates of Electron Transfer and S_N2 Reactions of 9-(Dialkylamino)fluorenide Ions with Alkyl Halides

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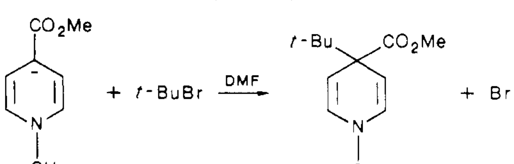
Abstract: Rate ratios for reactions of $PhCH_2Cl$ vs Ph_2CHCl with seven 9-(dialkylamino)fluorenide (9-R_2NFl^-) ions were measured in Me_2SO solution. Although the reaction sites in these ions are known to be highly congested and Ph_2CHCl is more sterically hindered than is $PhCH_2Cl$, the $k^{PhCH_2Cl}/k^{Ph_2CHCl}$ rate ratios for reactions with 9-R_2NFl^- ions in Me_2SO were all much lower (0.20–4.9) than for the less hindered 9-$MeFl^-$ or p-$MeOC_6H_4O^-$ ions (81 and 138, respectively). This suggested that the Ph_2CHCl reactions with 9-R_2NFl^- ions were occurring by single electron transfer (SET) mechanisms, despite the formation of high yields of S_N2-type products. This conclusion was supported by the observation of a close correspondence between SET rates (log k_{SET}), calculated by using the Marcus equation, and log k_{obsd} for reactions of 9-R_2NFl^- ions with both a known single electron acceptor, F_3CCH_2I, and with Ph_2CHCl and (p-$ClC_6H_4)_2CHCl$. Similar log k_{SET} vs log k_{obsd} comparisons for reactions of the 9-R_2NFl^- ions with $PhCH_2Cl$, c-$C_6H_{11}Br$, and n-BuBr revealed greater disparity.

The idea that, in principle, a concerted ("polar") S_N2 reaction can merge with a single electron transfer (SET) mechanism, wherein the product is formed by coupling of a geminate radical pair, has been recognized for many years.[1] In his recent definitive book on electron transfer reactions Eberson concludes, however, that it takes a very strong electron donor anion to effect a bimolecular aliphatic substitution reaction on an alkyl halide by an outer-sphere SET mechanism.[2] Nevertheless, he points out that this has been achieved for certain alkyl halides and that there is good reason to believe that this SET mechanism will merge with the concerted single electron shift S_N2 reaction, as has been suggested by several investigators.[3] Outer-sphere SET substitutions have been observed by Lund and Lund for reactions of t-BuBr with radical anions, $ArH^{\bullet-}$, and with carbanion **1**, which



1 **2** (1)

was generated electrochemically from 4-(methoxycarbonyl)-*N*-methylpyridinium iodide. Similar substitutions were also observed for reactions of **1** with 1-adamantyl and neopentyl bromides, but the less hindered ethyl, *n*-butyl, and *sec*-butyl bromides appeared to react by borderline mechanisms.[3]

In earlier papers[4] we have shown that reactions of 9-substituted fluorenide ions, 9-GFl^-, with $PhCH_2Cl$ are subject to rate-retarding steric effects, as G becomes more bulky along the series, Me, Et,

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Table I. Rates of Reactions of 9-Substituted Fluorenide Ions, 9-GFl$^-$, with Benzyl and Benzhydryl Chlorides

G	r[a]	pK_a	$E_{ox}(A^-)$[b]	k^{Ph_2CHCl}[c]	$k^{PhCH_2Cl}/k^{Ph_2CHCl}$[e]
Me	(0.0)	22.3	−0.480	0.609	81
$PhCH_2$	−0.10	21.4	−0.402	0.30	65
MeO		22.1	−0.574	0.28	51
4-MeC_6H_4		18.3	−0.318	−0.074[d]	12
Ph	−0.58	17.9	−0.278	0.057[d]	11
3-ClC_6H_4		16.85	−0.188	0.038[d]	6.8
4-$MeSO_2C_6H_4$		15.2	−0.097	0.015[d]	4.3
c-C_6H_{11}		23.0	−0.434	0.130	28
t-Bu	−2.6	24.35	−0.409	0.041	11.5
azetidinyl	−0.17	21.8	−0.865	8.19	2.7
pyrrolidinyl	−1.2	22.2	−0.805	3.48	0.83
Me_2N	−1.5	22.5	−0.660	0.267	4.9
piperidinyl	−1.6	22.5	−0.643	0.270	4.8
2-Me-piperidinyl		21.5	−0.598	0.062	1.2
2,2,6,6-Me_4-piperidinyl		18.3	−0.438	0.028	0.12
i-Pr_2N	−3.4	20.8	−0.485	0.0349	0.20

[a] In log units.[4] [b] Measured by cyclic voltammetry in Me_2SO with a Ag/AgI reference electrode; referenced to the aqueous standard hydrogen electrode (SHE) by adding −0.125 V. [c] M^{-1} s^{-1}; measured spectrophotometrically by the method described previously.[4a] [d] Reference 8a. [e] The rate data with $PhCH_2Cl$ are from ref 4, 5, 16, and 21.

i-Pr, *t*-Bu, and *i*-Pr_2N, that cause progressive rate decreases over a range of nearly 10^4. In contrast, a low sensitivity to the steric bulk of G was observed for reactions of 9-GFl$^-$ ions with two single-electron acceptors, 1,1-c-$C_6H_{10}(NO_2)Ts$[5] and F_3CCH_2I,[6] in authentic SET reactions. With each of these acceptors a plot of log k_{obsd} vs the oxidation potentials of the anions, $E_{ox}(A^-)$, was linear for reactions where the steric demands of G varied appreciably, e.g., G = Me, MeO, MeS, *t*-Bu, and R_2N. Furthermore, we have presented evidence in a preliminary account that rates of reactions of a series of 9-R_2NFl^- ions with F_3CCH_2I or Ph_2CHCl plot linearly with $E_{ox}(A^-)$. This led to the conclusion that both of these latter reactions were occurring by single electron transfer (SET) radical pair mechanisms, F_3CCH_2I reacting to give radical products and Ph_2CHCl reacting to give substitution products.[7] We now present a more complete account of these results, including an extension of the study to $(p\text{-}ClC_6H_4)_2CHCl$, *n*-BuBr, and c-$C_6H_{11}Br$.

Results and Discussion

Steric Effects in Reactions of 9-GFl$^-$ Ions with $PhCH_2Cl$ and Ph_2CHCl. The rates of reactions of 9-R_2NFl^- and other 9-GFl$^-$ ions with Ph_2CHCl are presented in Table I and are compared with rates of reactions with $PhCH_2Cl$.

The presence of the second Ph group in Ph_2CHCl should markedly increase steric hindrance to nucleophilic attack, relative to that with $PhCH_2Cl$. One would expect on steric grounds, therefore, to see large $k^{PhCH_2Cl}/k^{Ph_2CHCl}$ rate ratios in Table I. Indeed, the ratio with 9-MeFl$^-$ ion is 81, and a ratio of 138 has been observed for reactions of these chlorides with the less sterically hindered *p*-$MeOC_6H_4O^-$ ion.[8] For the first nine (miscellaneous) groups (G) in Table I the steric retardation factor, r (eq 2), for

$$r = \beta(\Delta pK_{HA}) - \log\,(k^{Me}/k^{G}) \qquad (2)$$

reactions with $PhCH_2Cl$ has been shown to increase from 0.0, for the reference group Me, to −2.6 (log units) for *t*-Bu (the Brønsted β = 0.31); for the second series of seven 9-R_2NFl^- ions the r values change from −0.17 for azetidinyl to −3.4 for *i*-Pr_2N.[4b] One would expect to see, for each of these series, a general increase in $k^{PhCH_2Cl}/k^{Ph_2CHCl}$ rate ratios and perhaps a precipitous increase when the r values are large, as for *t*-Bu and *i*-Pr_2N. Instead, there is a general tendency for the ratios to *decrease* for the first series; for the second series all the ratios are small, those for *t*-Bu and *i*-Pr_2N being 11.5 and 0.20, respectively. The reactions of 9-GFl$^-$ ions with $PhCH_2Cl$ and Ph_2CHCl gave good to high yields of S_N2-type substitution products in all cases tested.

In an earlier paper the trio of 9-GFl$^-$ ions, where G = Me, MeO, Me_2N, which have nearly the same basicity but progressively more negative $E_{ox}(A^-)$ values, was shown to give progressively faster rates with known SET acceptors. The trio was selected for this reason to serve as a test for SET characteristics in reactions with alkyl halides.[6] The test failed to reveal SET characteristics in reactions of the trio with $PhCH_2Cl$, however, the rate constants decreasing progressively along the series instead of increasing. Since the size of the rate constant decreases corresponded closely to rate constant decreases along the series G = CH_3, $MeCH_2$, Me_2CH, it was concluded that the order of rate constants for the S_N2 reactions with $PhCH_2Cl$ was determined by steric effects with no indication of a SET component. One would then expect the rate constant differences for S_N2 reactions of the trio with the more sterically hindered Ph_2CHCl to be exaggerated. Instead, the differences essentially disappear, the relative rates being 2.3, 1.1, and 1.0, respectively.

Evidence for Single Electron Transfer (SET) in Reactions of 9-R_2NFl^- Ions with Ph_2CHCl and $PhCH_2Cl$. In view of the evidence obtained earlier for a relatively low sensitivity to steric effects with single electron acceptors,[5,6] the results described above and in Table I suggest that $PhCH_2Cl$ and Ph_2CHCl are reacting by different mechanisms. As a first approximation, we assume that for $PhCH_2Cl$ the mechanism is essentially a concerted S_N2 reaction and as such is sensitive to steric effects. For Ph_2CHCl, we assume that the reactions with 9-GFl$^-$ ions are occurring by stepwise SET (radical pair) mechanisms that are relatively insensitive to steric effects. (An S_N1 mechanism is ruled out since the rates are first order in nucleophile as well as electrophile.)

The observation that the rates of reactions (k_{obsd}) of SET acceptors with 9-GFl$^-$, where G varies in size and structure, plot linearly with their $E_{ox}(A^-)$ values[5,6] and the results shown in Table I led us to examine reactions for a series of 9-R_2NFl^- ions as a possible test for SET in reactions with electrophiles. The 9-R_2NFl^- ions in this series do not differ appreciably in basicity (pK_{HA} = 22 ± 1.2) but have oxidation potentials that cover a considerable range (0.427 V or 9.8 kcal/mol). A Marcus-type plot of log k_{obsd} vs $E_{ox}(A^-)$ for a series of 9-R_2NFl^- ions reacting with F_3CCH_2I, a known SET acceptor, was indeed found to be reasonably linear,[7] and better linearity was observed for a plot for 9-R_2NFl^- ions reacting with Ph_2CHCl.[7] The fit was better for the latter plot because the kinetics were better. The rates were monitored in each instance by following the decrease in absorbance of the 9-R_2NFl^- ions. For F_3CCH_2I, the ln (abs_0/abs_T) vs time plots began to deviate from linearity after 1 half-life, probably because of interference from a strongly absorbing product species (9-$R_2NFl^{\bullet}$ or the like). On the other hand, the kinetics for the reactions with Ph_2CHCl remained linear for several half-lives, as is typical of S_N2 reactions of 9-GFl$^-$ ions with alkyl halides.

Additional support for a stepwise SET pathway for the reactions of this series of 9-R_2NFl^- ions iwth F_3CCH_2I and Ph_2CHCl was obtained by a comparison of the rate constants observed for these reactions with those calculated for SET by Eberson's method using the Marcus equation (eq 3).[9]

$$\log k_{SET} = \log k_d - \log \left\{1 + 0.2 \exp\left[\frac{\lambda}{4}\left(1 + \frac{\Delta G^\circ}{\lambda}\right)^2 / RT\right]\right\} \qquad (3)$$

The value of k_d in eq 3, the diffusion-controlled rate in Me_2SO, is taken as 3.3×10^9;[10] $\Delta G^\circ = 23.06[E_{rd} - E_{ox}(A^-)]$, where E_{rd}

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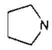
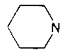
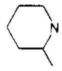
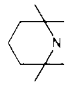
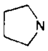
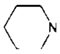
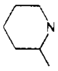
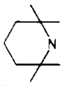
Table II. Comparison of Rates (k_{obsd}) with Expected Rates of Single Electron Transfer (log k_{SET}) for Reactions of 9-(Dialkylamino)fluorenide Ions, 9-R_2NFl^-, with F_3CCH_2I and Ph_2CHCl

	F_3CCH_2I[b]			Ph_2CHCl[d]		
NR^2	ΔG_0[a]	log k_{obsd}	k_{obsd}/k_{SET}[c]	ΔG_0[a]	log k_{obsd}	k_{obsd}/k_{SET}[c]
	−6.8	fast		−9.0	+0.91	0.34
	−5.4	fast		−7.6	+0.54	0.53
NMe_2	−2.1	+0.75	6.0	−4.3	−0.57	0.40
	−1.7	−0.28	8.3	−3.9	−0.57	0.55
	−0.6	−1.43	0.14	−2.9	−1.21	0.28
N(*i*-Pr)$_2$	+2.0	−1.50	1.1	−0.3	−1.45	1.4
	+3.0	−2.25	1.22	+0.8	−1.55	0.45

[a] In kcal/mol. [b] E_{rd} = 0.4 × (1.425) = −0.57;[23] λ = 60. Radical-reaction-type products are formed. [c] Calculated from eq 2. [d] E_{rd} = 0.4 × (1.185) = −0.474;[23] λ = 65. S_N2 products were obtained.

Table III. Comparison of Rates (k_{obsd}) with Expected Rates of Single Electron Transfer (k_{SET}) for Reactions of 9-R_2NFl^- with $(p\text{-}ClC_6H_4)_2CHCl$ and $PhCH_2Cl$

	$(p\text{-}ClC_6H_4)_2CHCl$[b]			$PhCH_2Cl$[d]		
NR^2	ΔG_0[a]	log k_{obsd}	k_{obsd}/k_{SET}[c]	ΔG_0[a]	log k_{obsd}	k_{obsd}/k_{SET}[c]
	−8.3	+1.36	2.0	−3.3	+1.35	71
	−7.0	+0.67	0.89	−2.0	+0.46	28
NMe_2	−3.6	+0.25	4.6	+1.8	+0.11	320
	−3.2	+0.39	8.7	+1.4	+0.27	300
	−2.2	−0.45	2.9	+2.8	−1.14	46
N(*i*-Pr)$_2$	+0.4	−1.20	4.4	+5.4	−2.16	44
	+1.5	−1.20	11	+6.5	−2.49	47

[a] In kcal/mol. [b] E_{rd} = 0.4 × (−1.259) = −0.503;[23] λ = 65. S_N2 products were obtained. [c] Calculated from eq 2. [d] E_{rd} = 0.52 + 0.20 = 0.72 (Eberson's E_{rd}[9] referenced to SHE_{aq}. S_N2 products were formed.

is the reduction potential of the electrophile and $E_{ox}(A^-)$ is the oxidation potential of the anion; both are determined for Me_2SO solution and referenced to the aqueous standard hydrogen electrode (SHE_{aq}). The E_{rd} values are taken from Eberson[9a] or calculated as described earlier.[7] The solvent and bond reorganization parameter, λ, is estimated from those for similar reactions reported elsewhere.[1,9a] Uncertainties of estimated λ and E_{rd} values cause k_{SET} calculations to be accurate to only 1 order of magnitude.

Eberson has used eq 3 to obtain k_{obsd}/k_{SET} ratios for 33 reactions of anionic nucleophiles with organic electron acceptors in order to estimate whether or not stepwise SET is feasible.[9a] The ratios vary from about 10^{-5} to 10^{28} or more; for 24 of these reactions the ratios were above 10^5, which places them in the "SET not feasible" class. Several organometallic reagents containing strongly basic carbanion or nitranion moieties were included, but examples of reactions of anions free of counterion effects were absent. Lund has filled this gap by carrying out an extensive study of reactions of aromatic radical anions, $ArH^{\bullet -}$, with simple alkyl halides and has found good fits for Marcus-type plots of log k vs $E_{ox}(A^-)$. Four $ArH^{\bullet -}$ ions with $E_{ox}(A^-)$ values (vs SHE_{aq}) ranging from −0.611 to −1.488 V reacting with *t*-BuBr were found to give progressively greater yields of substitution products as $E_{ox}(A^-)$ became more negative.[3a] Good yields of substitution products were also obtained from reactions of carbanion **1** with *t*-BuBr or neopentyl bromide, and it was concluded that the rate-limiting step in these reactions, as well as that of **1** with 1-adamantyl bromide, was an outer-sphere single electron transfer. The k_{obsd}/k_{SET} ratios for reactions of **1** with these bromides were 2.5, 1.3, and 0.8, respectively, compared to 170, 400, and 2500 for *sec*-BuBr, *n*-BuBr, and EtBr, respectively. In a later paper the reaction of **1** with $C_6H_5C(Me)(Et)Cl$ was reported to give k_{obsd}/k_{SET} = 1.3. The reaction is thus pure outer-sphere SET; PhCH(Me)Cl gave k_{obsd}/k_{SET} = 8.2, and the reaction was classified as borderline.[11]

The results of the application of Eberson-type calculations to the reactions of the series of 9-R_2NFl^- ions with F_3CCH_2I and Ph_2CHCl are shown in Table II. The value of λ was modeled after that used by Eberson for $PhCH_2Cl$ and Ph_3CCl,[7] and that for F_3CCH_2I was chosen by trial and error to give the best fit for the data. Examination of Table II shows that the k_{obsd}/k_{SET} ratios are near unity for the two reactions, indicating that both are reacting by SET mechanisms involving radical-pair intermediates, F_3CCH_2I giving radical-type products,[6] and Ph_2CHCl giving S_N2-type products. The results with F_3CCH_2I and Ph_2CHCl provide strong support for Eberson's method of SET calculation in that, for the first time, a family of anions has been used in a reaction known to occur by a SET mechanism, and the correspondence between k_{obsd} and k_{SET} is good over a considerable $E_{ox}(A^-)$ range. In reactions of this family, factors such as the strength of the bonds being formed and broken and the nature of the solvent and geometric reorganization are kept essentially constant.

There appears to be little prospect of trapping the $Ph_2CHCl^{\bullet -}$ anion radical, since its lifetime has been shown to be less than 20 ps,[12] corresponding to a rate constant of >5 × 10^{10} s^{-1}. It has been suggested that, in SET to Ph_2CHCl, the $Ph_2CH^\bullet$ radical and Cl^- ion are formed directly without the $Ph_2CHCl^{\bullet -}$ radical ion as an intermediary. The $PhCH_2^\bullet$ radical will also be difficult to trap since it is expected to dimerize at a diffusion-controlled rate. On the other hand, the 9-*i*-$Pr_2NFl^\bullet$ radical is persistent when formed in the reaction of 9-*i*-Pr_2NFl^- with F_3CCH_2I, presumably because it is relatively stable and dimerization is inhibited by steric hindrance. Additional support for the SET mechanism was obtained by observation of a peak at 450 nm, characteristic of the 9-*i*-$Pr_2NFl^\bullet$ radical,[6] in a reaction with Ph_2CHCl. The peak is not persistent under these conditions, however, presumably because of rapid coupling with the $Ph_2CH^\bullet$ radical. No indication of the presence of $(Ph_2CH)_2$ or $(9\text{-}R_2NFl)_2$ dimers was evident in the product NMR. This is not surprising since even if the $Ph_2CH^\bullet$ and 9-$R_2NFl^\bullet$ radicals escape from the cage, theory tells us that, if dimerization of one of the radicals is slow (as is expected for 9-$R_2NFl^\bullet$), the cross-coupling product will be overwhelmingly favored.[13]

The results for 9-R_2NFl^- ions reacting with Ph_2CHCl were confirmed by repeating the experiments with $(p\text{-}ClC_6H_4)_2CHCl$. Since the Hammett σ for *p*-Cl is +0.24 we expected E_{rd} with this chloride to be less negative than that of the parent, but the E_{rd} proved to slightly more negative. (Evidently the π-donor properties of the *p*-Cl substituent are more decisive in determining the size of E_{rd} than are its field–inductive acceptor properties.) The electron-transfer reactions with this acceptor are therefore a little less exergonic than with Ph_2CHCl. The k_{obsd}/k_{SET} ratios with this acceptor are generally larger than unity for this acceptor, instead of being smaller (Table III).

The results with the 9-R_2NFl^- ion family reacting with Ph_2CHCl and $(p\text{-}ClC_6H_4)_2CHCl$ agree well with those reported for carbanion **1** reacting with *t*-BuBr, 1-AdBr, *t*-$BuCH_2Br$,[3] and $C_6H_4C(Me)(Et)Cl$.[11] Carbanion **1** has an oxidation potential of −1.48 V (vs SHE_{aq}), which means that its potential is 0.615 V (14.2 kcal/mol) more negative than the best 9-R_2NFl^- ion donor and 1.042 V (24 kcal/mol) more negative than the worst. In

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(11) Lund, T.; Lund, H. *Acta Chem. Scand. Ser. B* **1987**, *B41*, 93–102.

(12) Simon, J. D.; Peters, K. S. *Organometallics* **1983**, *2*, 1867–1869.

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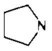
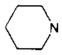
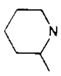
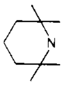
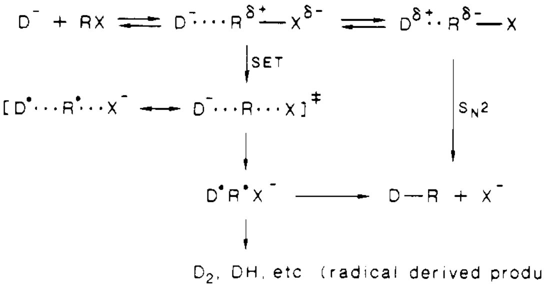
Table IV. Rate Constants for Reactions of 9-R_2NFl^- Ions with *n*-Butyl Bromide and Cyclohexyl Bromide

	n-BuBr[b]			*c*-$C_6H_{11}Br$[d]		
R_2N	ΔG_0[a]	log k_{obsd}	k_{obsd}/k_{SET}[c]	ΔG_0[a]	log k_{obsd}	k_{obsd}/k_{SET}[c]
	+3.3	+0.80	1600	−1.03	−0.250	3.1
					−0.277[e]	
	+4.7	+0.33	1700	+0.35	−0.777[e]	3.4
NMe_2	+8.1	−0.04	22000			
	+8.5	+0.01	32000	+4.08	−1.03	4.7
	+9.5	−1.24	4600	+5.11	−1.82	17
N(*i*-Pr)$_2$	+12.1	−2.62	2200	+7.7	−2.12[e]	95
	+13.2	−2.80	3100			

[a] In kcal/mol. [b] $E_{rd} = -0.82 - 0.20 = -1.01$ (Eberson's E_{rd}[9] referenced to SHE_{aq}); $\lambda = 62$ (Lund's $\lambda = 73$).[11] [c] Calculated from eq 1. [d] $E_{rd} = 0.4 \times (-2.05) = -0.82$ vs SHE_{aq};[23] $\lambda = 62$; S_N2 and E2 products were formed. [e] Results of C. A. Wilson.

Scheme I



reactions of **1** with $PhCH_2Cl$ and *p*-$MeOC_6H_4CH_2Cl$, k_{obsd}/k_{SET} ratios of 66 and 93, respectively, were reported,[11] which agree well with ratios obtained for reactions of $PhCH_2Cl$ with four of the 9-R_2NFl^- ions shown in Table III.

Our study of reactions of 9-R_2NFl^- ions was next extended to *n*-butyl and cyclohexyl bromides, which have E_{rd} potentials at least 100–300 mV more negative than that of $PhCH_2Cl$ (Table IV). The k_{obsd}/k_{SET} ratios with *n*-BuBr were 2–4 orders of magnitude higher than Lund's ratio for the reaction of **1** with *n*-BuBr. On the other hand, the k_{obsd}/k_{SET} ratios observed for the reactions of 9-c-$C_3H_6NFl^-$, 9-c-$C_4H_8NFl^-$, and 9-c-$C_5H_{10}NFl^-$ ions with c-$C_6H_{11}Br$ were similar to those found for reactions with (*p*-$ClC_6H_4)_2CHCl$ (Table III). It seems likely that the greater steric hindrance in the c-$C_6H_{11}Br$ electrophile may be favoring the SET reaction, a result that would be similar to that of Lund's in comparisons of k_{obsd}/k_{SET} ratios for *t*-BuBr, 1-AdBr, and Me_3CCH_2Br vs EtBr, *n*-BuBr, and *sec*-BuBr.[3a] It is noteworthy in this regard that, as will be brought out shortly, our ratios with c-$C_6H_{11}Br$ are 1 or 2 orders of magnitude smaller than Lund's with the less hindered *sec*-BuBr. The reactions of 9-R_2NFl^- ions with *n*-BuBr give high yields of substitution products, whereas those with c-$C_6H_{11}Br$ give a mixture of substitution and elimination products.

The k_{obsd} values for the reactions of 9-R_2NFl^- ions with Ph_2CHCl and (*p*-$ClC_6H_4)_2CHCl$, which are occurring by SET mechanisms, are compared graphically with those with $PhCH_2Cl$ in Figure 1. The gently sloping line is that calculated for the SET mechanism from eq 3. Figure 2 shows a similar comparison for the reactions with c-$C_6H_{11}Br$ and *n*-BuBr.

Mechanisms of Reactions of 9-R_2NFl^- Ions with Alkyl Halides. The mechanism for reaction of 9-GFl^- ions with F_3CCH_2I or Ph_2CHCl is assumed to occur by a rate-determining outer-sphere dissociative SET, as outlined in general terms in Scheme I. In the first step a molecular ion complex is formed. The binding of D^- to RX is weak, but a long-range SET can take place because $\Delta G°$ is in the range of +3 to −6.8 kcal/mol for reactions of 9-R_2NFl^- ions with F_3CCH_2I and +0.8 to −9 kcal/mol with Ph_2CHCl (Table II). The electrostatic attraction in the transition states for such outer-sphere SETs is of the order of 1 kcal/mol according to the Marcus theory.[1] For reactions of 9-$PhCH_2Fl^-$ with F_3CCH_2I, disproportionation products from the 9-$PhCH_2Fl^\bullet$ radical and products from the attack of $F_3CCH_2^\bullet$ radicals on the fluorene ring have been identified.[6] For reactions of a variety of 9-GFl^- ions with Ph_2CHCl, good yields of substitution products have been obtained, but the calculations in Table II indicate that with 9-R_2NFl^- ions the reactions occur by an SET mechanism (Table II). Similar results are obtained in reactions of 9-R_2NFl^- ions with (*p*-$ClC_6H_4)_2CHCl$ (Table III).

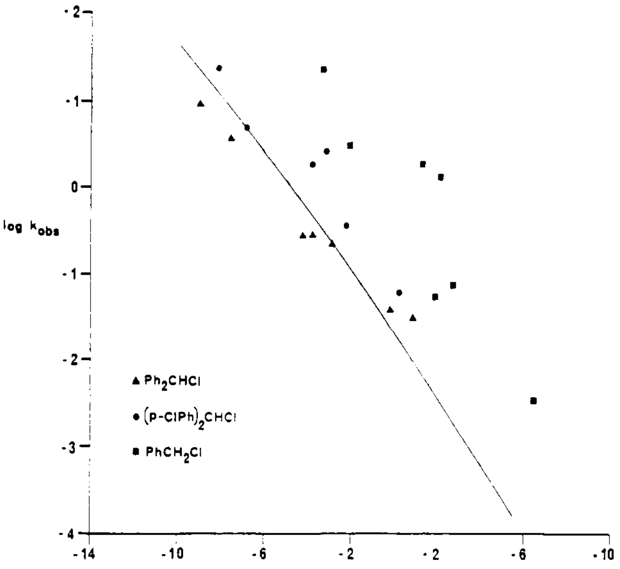


Figure 1. Marcus plot of log k_{obsd} for reaction of 9-(dialkylamino)fluorenide ions with Ph_2CHCl, (*p*-$ClC_6H_4)_2CHCl$, and $PhCH_2Cl$ vs their free energy of electron transfer ($\Delta G°$). The solid line represents part of the expected Marcus parabola for $\lambda = 65$.

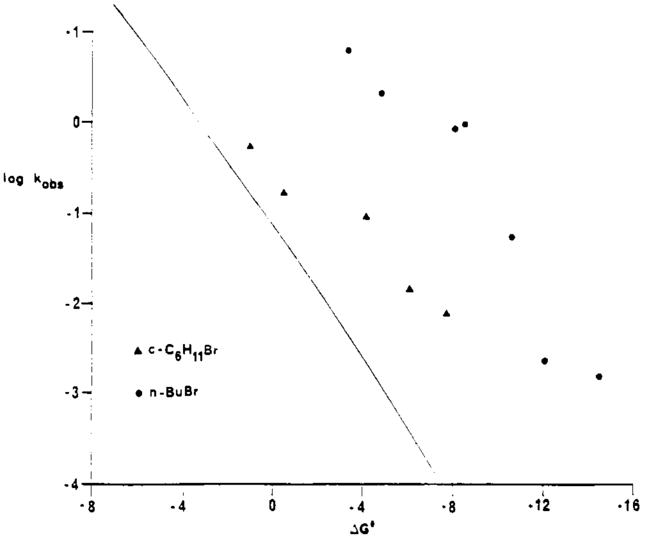


Figure 2. Marcus plot of log k_{obsd} for reaction of 9-(dialkylamino)fluorenide ions with c-$C_6H_{11}Br$ and *n*-BuBr vs their free energy of electron transfer ($\Delta G°$). The solid line represents part of the expected Marcus parabola for $\lambda = 62$.

Reaction of $PhCH_2Cl$ with 9-R_2N-Fl^- ions give k_{obsd}/k_{SET} ratios of 30–320. The calculations appear to indicate that these reactions, as well as those with c-$C_6H_{11}Br$ (Table IV), are in a borderline region. Since the reactions of 9-R_2NFl^- ions with $PhCH_2Cl$ show larger steric effects than do the reactions with the more sterically demanding Ph_2CHCl electrophile, it is clear that the former are more S_N2 in nature. The reactions of 9-R_2NFl^- ions with *n*-BuBr are further in the endergonic region and the k_{obsd}/k_{SET} ratios are an order of magnitude larger. Reactions that are too endergonic to proceed by the SET pathway can be accommodated in terms of Scheme I by assuming formation of a second ion–molecule complex with a stronger electrostatic attraction bringing the reactants into a closer proximity for reaction. This would require desolvation and some molecular reorganization, but the energy required can be more than repaid by the relatively low barrier provided by the synchronous SET process.[14] It seems likely that when k_{obsd}/k_{SET} ratios are near unity, or below, the radical pair mechanism will obtain, and that when the ratio is 10^2 or above, the concerted S_N2 mechanism will obtain. In the borderline region the two mechanisms may be in competition or, as proposed elsewhere,[2,15] hybrid or merged mechanisms may occur wherein the distance of approach of D^- and RX is intermediate to the stepwise and concerted SET extremes, resulting in partial bonding between $D^•$ and $R^•$ as electron transfer occurs.

Summary and Conclusions

A series of seven 9-R_2NFl^- ions wherein the R_2N groups are known to possess steric retardation rate (*r*) factors as much as 3.4 orders of magnitude *greater* than that of Me were found to give rate ratios, $k^{PhCH_2Cl}/k^{Ph_2CHCl}$, that were all at least 1 order of magnitude *smaller* than that of Me. We conclude that the 9-R_2NFl^- ions are reacting with the more sterically demanding Ph_2CHCl electrophile by a single electron transfer (SET) mechanism. This conclusion was supported by (a) the observation of near unity rate ratios of k_{obsd} values to k_{SET}, the rate constant calculated by using the Marcus equation, and (b) by a reasonable fit to a Marcus plot (Figure 1). High yields of substitution products were formed in reactions of 9-GFl^- ions with Ph_2CHCl as well as $PhCH_2Cl$. The k_{obsd}/k_{SET} ratios for 9-R_2NFl^- ions with F_3CCH_2I, a known SET acceptor, and $(p\text{-}ClC_6H_4)_2CHCl$ were comparable. For substitution reactions of $PhCH_2Cl$ and substitution/elimination reactions of c-$C_6H_{11}Br$ with 9-R_2NFl^- ions, the k_{obsd}/k_{SET} ratios were, with few exceptions, larger, and the fit with a Marcus plot were poorer (Figures 1 and 2). The mechanisms for these reactions appear to be in a borderline SET–S_N2 region. The k_{obsd}/k_{SET} ratio for 9-R_2NFl^- ions reacting with *n*-BuBr was 10^3–10^4, which places the mechanism in the time-honored concerted S_N2 category.

Experimental Section

The methods used for determination of rate constants[16] and cyclic voltammetry measurements[17] have been described in earlier publications. ^1H NMR spectra were obtained with a Varian EM-390 spectrometer and chemical shifts are reported relative to tetramethylsilane. Melting points were measured with a Thomas-Hoover capillary apparatus and are uncorrected. Mass spectra were run by H. L. Hung on a HP5984 GC/MS system.

Materials. Benzyl chloride, benzhydryl chloride, 2,2,2-trifluoroethyl iodide, *n*-butyl bromide, and cyclohexyl bromide were obtained commercially and purified by distillation prior to use.

4,4′-Dichlorobenzhydryl chloride was prepared from the reaction of 4,4′-dichlorobenzhydrol with thionyl chloride (1.2 equiv) in refluxing benzene for 1 h. The product was recrystallized from ether and washed with hexane: mp 60–60.5 °C (lit.[18] mp 63 °C); ^1H NMR ($CDCl_3$) δ 6.0 (s, 1 H), 7.22 (br s, 10 H). It should be noted that use of this compound (despite proper precautions against exposure) caused an allergic response in one researcher (J.A.H.) resembling chloracne, which Sax[19] describes for chlorinated diphenyls. A previous researcher experienced no such problems.

Preparation of the 9-(dialkylamino)fluorenes was described in a preceding paper.[4b]

Product Studies. Reactions of 9-GFl^- ions with Ph_2CHCl, $PhCH_2Cl$, *n*-BuBr, and other simple alkyl halides have been shown to yield S_N2 products in numerous earlier studies.[4,8,16,20] In particular, 9-c-$C_4H_8NFl^-$ was shown to give 70% S_N2 product and 30% 9-c-C_4H_8NFlH (E2 product) when reacted with c-$C_6H_{11}Br$.[21] Additional studies were carried out for cases where products other than expected S_N2 products might be possible and are reported below.

Reaction of 9-Me_2NFl^- Ion with Ph_2CHCl. 9-(Dimethylamino)fluorene (112 mg, 5.4 × 10^{-4} mol) was reacted with 1 equiv of $CH_3SOCH_2^-K^+$ and then with 1 equiv of benzhydryl chloride for 10 min. The reaction was quenched with water and the product was extracted with ether. Residual Me_2SO was removed from the ether layer by multiple washing with water. After drying of the layer with anhydrous magnesium sulfate, the ether was removed under reduced pressure, giving 198 mg (98%) of the crude substitution product: mp 118–126 °C; ^1H NMR ($CDCl_3$) δ 2.25 (s, 6 H), 5.25 (s, 1 H), 7.0–7.5 (m, 18 H); MS, *m/e* 375 (24.9), 374 (molecular ion, 81.1), 374 (81.1), 371 (20.3), 208 (57.4), 192 (39.4), 165 (100); recrystallization from ethanol gave material with mp 136–136.5 °C. (The ^1H NMR ($CDCl_3$) of the recrystallized material was identical with that of the crude product.) Anal. Calcd for $C_{28}H_{25}N$: C, 89.55; H, 6.71; N, 3.74. Found: C, 89.43; H, 6.64; N, 3.77.

Reaction of 9-c-$C_4H_8NFl^-$ Ion with Ph_2CHCl. A 113-mg (4.8 × 10^{-4} mol) sample of 9-pyrrolidinylfluorene was treated with 1 equiv of $CH_3SOCH_2^-K^+$ in Me_2SO and reacted for 10 min with 1 equiv of benzhydryl chloride. Workup gave 161 mg (83%) of the crude substitution product: mp 129–132 °C; ^1H NMR ($CDCl_3$) δ 1.5–1.7 (br, 4 H), 2.4–2.7 (br t, 4 H), 5.25 (s, 1 H), 6.9–7.6 (m, 18 H); MS, *m/e* 403 (1.2), 402 (molecular ion, 3.0), 332 (99.2), 234 (100); recrystallization from ethanol gave material with mp 135–136 °C. The ^1H NMR ($CDCl_3$) of recrystallized material was identical with that of the crude product.

Reaction of 9-*i*-Pr_2NFl^- with Ph_2CHCl. A 39-mg (1.5 × 10^{-4} mol) sample of 9-(diisopropylamino)fluorene was reacted with 1 equiv of $CH_3SOCH_2^-K^+$ and 1 equiv of benzhydryl chloride for 24 h. Workup gave 65 mg (92%) of the crude substitution product as a semisolid: ^1H NMR ($CDCl_3$) δ 1.0 (d, 12 H), 3.45 (m, 2 H), 5.9 (s, 1 H), 7.1–8.2 (m, 18 H); MS, *m/e* 432 (3.7), 431 (molecular ion, 9.8), 416 (21.4), 331 (100), 165 (49).

Reaction of 9-*p*-$MePhFl^-$ Ion with Ph_2CHCl. 9-*p*-Tolylfluorene (208 mg, 8.1 × 10^{-4} mol) was reacted[8a] with 1 equiv of $CH_3SOCH_2^-K^+$ and then with 1 equiv of benzhydryl chloride for 2 h. Workup gave 330 mg (97%) of crude substitution product: mp 164–178 °C; ^1H NMR ($CDCl_3$) δ 2.2 (s, 3 H), 5.6 (s, 1 H), 6.5–7.5 (m, 22 H). Recrystallization from hexane/ethyl acetate gave material with mp 176–177 °C.

Reaction of 9-$PhFl^-$ Ion with $(p\text{-}ClC_6H_4)_2CHCl$. 9-Phenylfluorene (243 mg, 1.0 × 10^{-3} mol) was reacted[22] with 1 equiv of $CH_3SOCH_2^-K^+$ and then 1 equiv of 4,4′-dichlorobenzhydryl chloride for 1.5 h. Workup gave 472 mg (92%) of crude substitution product: ^1H NMR ($CDCl_3$) δ 5.5 (s, 1 H), 6.4–7.8 (m, 21 H); MS, *m/e* 477 (1.2), 241 (100), 237 (44.3), 235 (68.5); recrystallization (ethanol/hexane) gave a material with mp 176.5–177.5 °C.

Reaction of 9-*i*-Pr_2NFl^- Ion with *n*-BuBr. 9-(Diisopropylamino)fluorene (94 mg, 3.5 × 10^{-4} mol) was reacted with 1 equiv of $CH_3SOCH_2^-K^+$ and then with 1 equiv of *n*-butyl bromide for 24 h. Workup gave 94 mg (82%) of the substitution product as a viscous oil: ^1H NMR ($CDCl_3$) δ 0.9 (d, 12 H), 1.2–2.3 (br, 9 H), 3.6 (m, 2 H), 7.1–7.8 (m, 8 H); MS, *m/e* 265 (22.8), 264 (100), 222 (49.6), 165 (33.9).

Reaction of 9-c-$C_4H_8NFl^-$ Ion with *n*-BuBr. 9-Pyrrolidinylfluorene (32.2 mg, 1.4 × 10^{-4} mol) was reacted with 1 equiv of $CH_3SOCH_2^-K^+$ and then with 1 equiv of *n*-butyl bromide for 18 h. Workup gave 39.8 mg (85%) of substitution product as a viscous oil: ^1H NMR ($CDCl_3$) δ 0.6–0.9 (m, 5 H), 1.0–1.3 (m, 2 H), 1.5–1.7 (m, 4 H), 2.15–2.35 (m, 2 H), 2.4–2.6 (m, 4 H), 7.15–7.8 (m, 8 H); MS, *m/e* 291 (molecular ion, 3.0), 234 (100), 165 (13.7).

Reaction of 9-*i*-Pr_2NFl^- Ion with c-$C_6H_{11}Br$. 9-(Diisopropylamino)fluorene (80.1 mg, 3.0 × 10^{-4} mol) was reacted with 1 equiv of $CH_3SOCH_2^-K^+$ and then with 1 equiv of cyclohexyl bromide for 24 h. Workup gave 90.9 mg of product which was assigned by NMR as 50%

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(14) For a recent discussion of the importance of "critical distance" in chemical reactions, see: (a) Menger, F. M. In *Nucleophilicity*; Harris, J. M., McManus, S. P., Eds.; Advances in Chemistry 215, American Chemical Society: Washington, DC, 1987; Chapter 14. (b) Mengr, F. M. *Acc. Chem. Res.* **1985**, *18*, 128–134.

(15) Pross, A.; Shaik, S. S. *Acc. Chem. Res.* **1983**, *16*, 363–370.

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(17) Bordwell, F. G.; Bausch, M. J. *J. Am. Chem. Soc.* **1986**, *108*, 1979–1985.

(18) Norris, J. F.; Banta, C. *J. Am. Chem. Soc.* **1928**, *50*, 1808–1812.

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(20) Bordwell, F. G.; Mrozack, S. R. *J. Org. Chem.* **1982**, *47*, 3802–3803.

(21) Wilson, C. A., unpublished results.

(22) Mrozack, S. R. Ph.D. Dissertation, Northwestern University, 1982.

(23) The observed E_{rd}, measured as a peak potential (E_p), has been multiplied by 0.4 to correct for the anionic shift caused by the rapid follow reaction. This fraction is patterned after the estimates of Eberson, which indicate that $E_{1/2}$ is reduced by 30–40% in Me_2SO or DMF for active halides, including $CH_2{=}CHCH_2Cl$, $CH_2{=}CHCH_2Br$, $PhCH_2Cl$, $PhCH_2Br$, and *t*-BuBr.[9c]

S_N2-type substitution product and 50% 9-*i*-Pr_2NFlH (from an elimination reaction): ^1H NMR ($CDCl_3$) δ 1.0–2.0 (m, 18.2 H), 2.9 (br, 2 H), 4.95 (s, 0.5 H), 7.2–7.8 (m, 8 H); MS, *m/e* 348 (1.3), 347 (substitution molecular ion, 3.1), 265 (19.2), 265 (elimination molecular ion, 61.7), 247 (30.6), 222 (36.0), 165 (100).

UV/Vis Spectra of 9-*i*-Pr_2NFl^- + Ph_2CHCl Reaction. The anion of 9-(diisopropylamino)fluorene has been shown to have three peaks (λ_{max} = 479, 510, 556 nm) in Me_2SO while the corresponding radical has a peak at 450 nm.[21] UV/vis spectra taken at various points during the reaction of *i*-Pr_2NFl^- ion with benzhydryl chloride showed the appearance of a small peak at 450 nm in addition to the three anion peaks. However, unlike reactions of this anion with electron acceptors ($PhSO_2CH_2Cl$, c-$C_6H_{10}(NO_2)Ts$, and F_3CCH_2I), the radical peak is not persistent and a colorless solution results when all of the anion absorbance has dissipated, presumably because of coupling of the *i*-$Pr_2NFl^\bullet$ radical with the $Ph_2CH^\bullet$ radical.

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Registry No. 9-$MeFl^-$, 31468-21-0; 9-$PhCH_2Fl^-$, 53629-11-1; 9-$MeOFl^-$, 71805-70-4; 9-(4-MeC_6H_4)Fl^-, 42730-14-3; 9-$PhFl^-$, 31468-22-1; 9-(3-ClC_6H_4)Fl^-, 73872-45-4; 9-(4-$MeSO_2C_6H_4$)Fl^-, 73872-44-3; 9-c-$C_6H_{11}Fl^-$, 117959-61-2; 9-*t*-$BuFl^-$, 73838-69-4; 9-c-$C_3H_6NFl^-$, 111933-70-1; 9-c-$C_4H_8NFl^-$, 111933-71-2; 9-Me_2NFl^-, 83936-70-3; 9-c-$C_5H_{10}NFl^-$, 111933-72-3; 9-(2-Me-c-C_5H_9N)Fl^-, 111933-73-4; 9-(2,2,6,6-Me_4-c-C_5H_6N)Fl^-, 111933-74-5; 9-*i*-Pr_2NFl^-, 109495-02-5; Ph_2CHCl_2, 90-99-3; $PhCH_2Cl$, 100-44-7; F_3CCH_2I, 353-83-3; (*p*-ClC_6H_4)$_2CHCl$, 782-08-1; *n*-BuBr, 109-65-9; c-$C_6H_{11}Br$, 108-85-0; 9-Me_2NFl, 53156-46-0; 9-Ph_2CH-9-Me_2NFl, 117959-62-3; 9-c-C_4H_8NFl, 7596-59-0; 9-Ph_2CH-9-c-C_4H_8NFl, 117959-63-4; 9-*i*-Pr_2NFl, 109495-00-3; 9-Ph_2CH-9-*i*-Pr_2NFl, 117959-64-5; 9-(4-MeC_6H_4)Fl, 18153-43-0; 9-Ph_2CH-9-(4-MeC_6H_4)Fl, 117959-65-6; 9-PhFl, 789-24-2; 9-(*p*-ClC_6H_4)$_2CH$-9-PhFl, 117959-66-7; 9-Bu-9-*i*-Pr_2NFl, 117959-67-8; 9-c-C_6H_{11}-9-*i*-Pr_2NFl, 117959-69-0; 9-*i*-$Pr_2NFl^\bullet$, 117959-70-3; 4,4′-dichlorobenzhydrol, 90-97-1.

Synthesis of (2*R*,3*R*)- and (2*S*,3*S*)-[2,3-$^2H_2$]Oxirane and Application of It to the Synthesis of Chirally Labeled Homoserine[†]

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Abstract: (2*R*,3*R*)- and (2*S*,3*S*)-[2,3-$^2H_2$]oxirane have been synthesized from 2-propynol, the key step being the asymmetric epoxidation of (*E*)-3-(triphenylsilyl)-2-propenol. To determine the enantiomeric purities of the oxiranes, they were reacted with phenyllithium, and the resulting 2-phenylethanol samples were converted to esters of (1*S*)-(−)-camphanic acid. ^2H NMR analysis (in the presence of Eu(dpm)$_3$) showed that (*R*)- and (*S*)-oxirane had ee values of 92% and 94%, respectively. The utility of (2*R*,3*R*)- and (2*S*,3*S*)-[2,3-$^2H_2$]oxirane as chiral labeling synthons was demonstrated by a two-step synthesis of chirally labeled homoserine lactone, which was resolved chromatographically as its *N*-(3,5-dinitrobenzoyl) derivative. The diastereomeric purity of the latter was assessed by ^1H NMR. Acid hydrolysis of (2*R*,3*S*,4*S*)-*N*-benzoyl[3,4-$^2H_2$]homoserine lactone resulted in extensive epimerization at C-4 of the lactone. An ^{18}O-labeling experiment failed to support a mechanism involving amide participation. It is concluded that the lactone was hydrolyzed by an unprecedented $A_{AL}2$ mechanism.

In many cases, syntheses of chirally labeled compounds are quite long, owing to the limited number of reagents and stereoselective reactions by which isotopic labels can be introduced.[1-3] While this has been true in our own work, in one recent instance it was clear that the necessary labeled substrates could be made economically by using a divergent route in which chirally labeled oxirane would serve as a common synthetic intermediate.

In this paper, we report the details of our synthesis and analysis of (2*R*,3*R*)- and (2*S*,3*S*)-[2,3-$^2H_2$]oxirane, including improvements over the methods that we have described in a preliminary communication.[4] The *general* utility of chirally labeled oxirane is also demonstrated by the synthesis of homoserine that is chirally labeled at carbons 3 and 4.[5] In addition, in the course of the homoserine synthesis, a mechanistically unprecedented acid-catalyzed epimerization at homoserine C-4 was observed.

Results

Synthesis and Analysis of Chirally Labeled Oxirane. The synthesis of chirally labeled oxirane (Scheme I) begins with 3-(triphenylsilyl)-2-propynol,[6,7] which is readily available from propargyl alcohol.[6] Reduction of the triple bond with lithium aluminum deuteride,[8] using deuterium oxide to quench the reaction, leads to (*E*)-3-(triphenylsilyl)-2-[2,3-$^2H_2$]propenol.[6,9] This labeled allylic alcohol is epoxidized by using a modified Sharpless procedure,[10,11] with (+)- and (−)-diisopropyl tartrate (DIPT) giving

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[†] C.-K.H.'s portion of these studies was performed in partial fulfillment of the requirements for the Ph.D. degree from the Department of Chemistry, The Catholic University of America, Washington, DC 20064.

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