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Effect of Allylic Groups on S_N2 Reactivity

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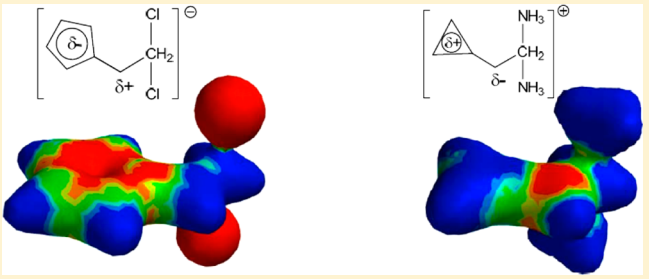
Supporting Information

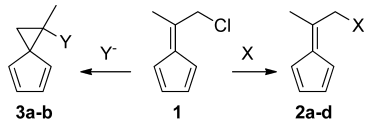
ABSTRACT: The activating effects of the benzyl and allyl groups on S_N2 reactivity are well-known. 6-Chloromethyl-6-methylfulvene, also a primary, allylic halide, reacts 30 times faster with KI/acetone than does benzyl chloride at room temperature. The latter result, as well as new experimental observations, suggests that the fulvenyl group is a particularly activating allylic group in S_N2 reactions. Computational work on identity S_N2 reactions, e.g., chloride$^-$ displacing chloride$^-$ and ammonia displacing ammonia, shows that negatively charged S_N2 transition states (tss) are activated by allylic groups according to the Galabov–Allen–Wu electrostatic model but with the fulvenyl group especially effective at helping to delocalize negative charge due to some cyclopentadienide character in the transition state (ts). In contrast, the triafulvenyl group is deactivating. However, the positively charged S_N2 transition states of the ammonia reactions are dramatically stabilized by the triafulvenyl group, which directly conjugates with a reaction center having S_N1 character in the ts. Experiments and calculations on the acidities of a variety of allylic alcohols and carboxylic acids support the special nature of the fulvenyl group in stabilizing nearby negative charge and highlight the ability of fulvene species to dramatically alter the energetics of processes even in the absence of direct conjugation.



INTRODUCTION

Fulvenes constitute a fascinating class of cross-conjugated olefins, and since their first synthesis by Thiele in 1900[1] they have commanded considerable interest due their diverse reactivities.[2] Our own efforts in this area focused mainly on the development of new methods for their synthesis,[3−6] their cycloaddition chemistry, and in particular, their reactions with singlet oxygen.[7−11] In the course of our studies, we found that the fulvenyl unit exerts a considerable electron-withdrawing effect on alkyl, aryl, and vinyl groups attached to the exocyclic double bond (C6), though our findings have been qualitative to date. Though the dipole moment of fulvenes is not particularly large in magnitude, these compounds are highly polarizable due to the aromatic character the polarization of the exocyclic π-system imparts to the cyclopentadienyl ring.[12] The extent of this polarization is manifested in the relatively more downfield shift of the protons on C6 in the NMR spectra,[13] as well as the ease of attack of various, mostly hard nucleophiles at the exocyclic double bond.[14] We previously tested the competing reactivities of a variety of nucleophiles toward C6 vs C7 carrying a leaving group on 6-chloromethyl-6-methylfulvene, whereas thiolate, azide, and thiocyanate ions[3a] and benzylamine[3b] undergo S_N2 attack at the chloromethyl group in **1**, and CN^- and CH_3Li[3a] exclusively attack C6, giving rise to spiro[2.4]hepta-4,6-diene derivatives (Scheme 1).[3] Recently, we have extended these reactions to competing C6 vs C7 attacks by various Michael donors.[15]

Scheme 1. Competitive Additions of Nucleophiles onto 1



3a-b **1** **2a-d**

Y = a) CN, b) CH_3(from MeLi)

X = a) N_3^-, b) SCN^-, c) PhS^-, d) $PhCH_2NH_2$[3b]

Herein, we report our results on our quest to quantitate the projected electron-withdrawing effect of the fulvenyl group by means of kinetic and computational studies.

S_N1 Reactivity. As a further test to assess the electron-withdrawing effect of the fulvenyl unit, 6-chloromethyl-6-methylfulvene (**1**) was subjected to S_N1 conditions using $AgNO_3$ in aqueous acetone. Even under forcing conditions (reflux), the corresponding alcohol **4** was not formed; instead,

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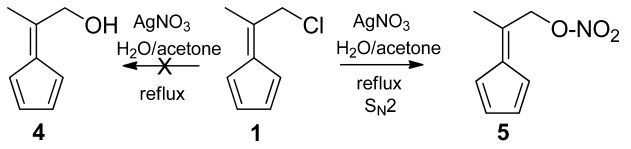
the nitrate ester **5** was isolated from the reaction mixture in low yield (5%) (Scheme 2). The reluctance of **1** to form an allylic

Scheme 2. Failed Attempt To Effect an S_N1 Reaction on 1



carbocation even with Ag^+ attests to the extent of destabilization exerted on the developing positive charge by adjacent the fulvenyl ring; instead the nitrate ion, though a very weak nucleophile, effects an S_N2 displacement at the fulvenyl C7.

S_N2 Reactivity. Prompted by the reaction chemistry described above, we have carried out a kinetics study probing the effect of the fulvenyl group on S_N2 reactivity. The kinetics study for each substrate was conducted in an NMR tube in acetone-d_6 solution. Table 1 shows our experimental second-order rate constants for the reaction of benzyl chloride and 6-(chloromethyl)-6-methylfulvene with potassium iodide in acetone at 23 ± 1 °C. A second-order constant for the benzyl chloride reaction is reported as 2.15×10^{-3} M^{-1} s^{-1} at 25 °C by Conant and Kirner.[16] The rate constant ratio, 2.15/1.5 = 1.4, can be ascribed to the difference in temperatures. We consider the two measurements to be in satisfactory agreement. The 6-methylfulvenyl substrate is seen to be more reactive than benzyl chloride by a factor of approximately 30, a significant activating effect for an all-hydrocarbon group. The rate ratio amounts to a $\Delta\Delta G^{\ddagger}$ of 2.0 kcal/mol.

Table 1. Experimental Second-Order Rate Constants for the Reaction of Benzyl and 6-Methylfulvenyl Chlorides with Potassium Iodide in Acetone at Room Temperature[a]

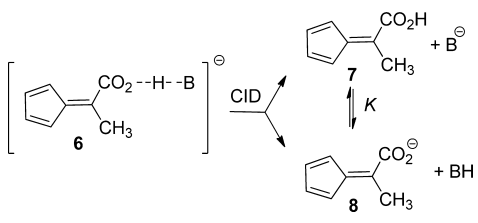
substrate	k (M^{-1} s^{-1})
benzyl chloride[b]	1.5×10^{-3}
6-chloromethyl-6-methylfulvene (**1**)	4.0×10^{-2}

[a]Approximately 23 °C. Reactions were run under pseudo-first-order conditions: $[\text{substrate}]_0$ = 0.20 M and $[\text{KI}]_0$ = 0.01 M. The rate of appearance of product was monitored by ^{1}HNMR. [b]Conant, J. B.; Kirner, W. R. *J. Am. Chem. Soc.* **1924**, *46*, 232−252. Lit. 2.15×10^{-3} M^{-1} s^{-1} at 25 °C using a titrimetric method.

GAS-PHASE PROTON AFFINITY MEASUREMENT

The proton affinity of 6-methylfulvene-6-carboxylate (**8**) was measured using the Cooks kinetic method; see Scheme 3.[17] In short, proton-bound complexes of 6-methylfulvene-6-carboxylate and reference bases were formed by electrospray ionization (ESI) and trapped in a quadrupole ion trap mass spectrometer. The desired ions were mass selected and then subjected to collision-induced dissociation (CID), which led to fragmentation of the complex and the formation of a free acid and an anion (Scheme 3). In this approach, it is assumed that the product distribution reflects the difference in proton affinities of the partners in the complex (i.e., K). In the present study, the proton affinity of 6-methylfulvene-6-carboxylate was tested against 2-nitrobenzoate (PA = 332 kcal/mol), 2-cyanophenoxide (PA = 335 kcal/mol), and 4-(trifluoromethyl)-phenoxide (PA = 337 kcal/mol). With 2-nitrobenzoate, CID only led to the reference base and with 4-(trifluoromethyl)-phenoxide; CID gave mainly 6-methylfulvene-6-carboxylate. CID of the complex with 2-cyanophenoxide gave mainly the phenoxide. These data suggest that 6-methylfulvene-6-carboxylate has a proton affinity of 336 ± 3 kcal/mol.

Scheme 3. Cooks Kinetic Method



Computational Results and Discussion. To investigate the sources of the fulvenyl effect and to probe the activating influence of allylic and benzylic groups on S_N2 reactions generally, we have carried out ab initio calculations with the G3MP2 composite approach and at the MP2(FC)/6-311+G** level on several allylic and nonallylic substrates and transition states (tss); Figure 1.

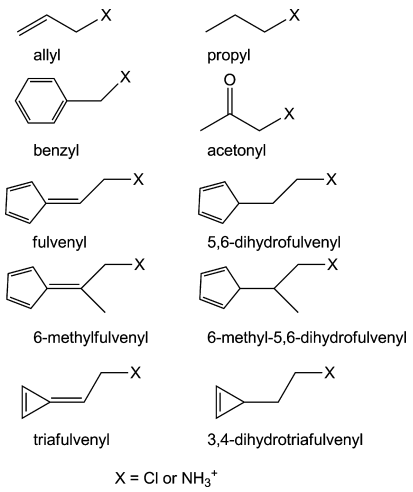


Figure 1. Substrates in the S_N2 computational study.

Table 2 lists calculated G3MP2 enthalpies of activation for the S_N2 identity reactions of chloride ion with propyl chloride and with four other primary alkyl chlorides. Each of the allylic chlorides is experimentally activated relative to the saturated analogues.[18] Also listed there are results for the identity reactions of some allylic primary alkyl ammonium ions with ammonia along with their nonallylic counterparts.

Alkyl Chlorides. The calculated $\Delta\Delta H^{\ddagger}$ value comparing the 6-methylfulvenyl chloride with benzyl chloride is seen to be 4.6 kcal/mol, somewhat greater than the experimental solution phase $\Delta\Delta H^{\ddagger}$ value. Additionally, calculated activation enthalpies for seven other primary alkyl chlorides, three allylic and four nonallylic, are given. The activation enthalpies are all small, even negative in three cases, consistent with the expected contribution of stabilization energy due to ion−molecule complexation of chloride with the R−Cl substrates. All transition states for the unsaturated R groups have geometries in which the Cl−C−Cl axis is perpendicular to the atomic framework of the alkyl groups; thus, the possibility exists, in principle, for π-conjugation with the unsaturated parts of those groups for vinyl, phenyl, 6-methylfulvenyl, fulvenyl, and

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Table 2. Calculated Enthalpies of Activation for Identity Substitution Reactions of Alkyl Chlorides with Chloride$^-$ and of Alkylammonium Ions with Ammonia[a]

alkyl group	$\Delta H^{\ddagger}$ (kcal/mol)	$i\nu^b$ (ts) (cm^{-1})
chlorides		
allyl	1.2	328
ally, perp[c]	(+4.5)[c]	386, 106
propyl	2.3	360
propyl, perp[c]	(+4.9)[c]	333, 72
benzyl	−1.3	319
fulvenyl	−4.2	354
5,6-dihydrofulvenyl	0.1	367
6-methylfulvenyl	−5.9	357
6-methyl-5,6-dihydrofulvenyl	1.3	346
triafulvenyl	3.0	369
3,4-dihydrotriafulvenyl	1.9	353
acetonyl	−7.1	425
ammonium ions		
allyl	12.1	393
propyl	16.3	470
fulvenyl	10.5	278
5,6-dihydrofulvenyl	15.0	474
triafulvenyl	0.3	219
triafulvenyl (MP2/6-311+G**)	3.2	219
triafulvenyl intermediate[d]	3.2	
triafulvenyl intermediate[d] (MP2/6-311G**)	1.5	
3,4-dihydrotirafulvenyl	17.2	464
heptafulvenyl[e]	NA	NA
7,8-dihydroheptafulvenyl	16.1	455

[a]Enthalpies calculated at the G3MP2 level except as noted. [b]The imaginary frequencies ($i\nu$) correspond to the S_N2 reaction coordinate in each case. Assuming that the entropies of activation for the benzyl chloride and 6-chloromethylfulvene reactions are very similar, the $\Delta\Delta H^{\ddagger}$ = 2.9 kcal/mol corresponds to a factor of 134 favoring the fulvenyl substrate. [c]These enthalpies, calculated at the MP2/6-311+G** level, are the *differences* in the transition-state enthalpies for an approximately 90° rotation about the C_α−C_β bond as, thus, are the enthalpies of activation for rotation about this bond in the ts. These differences could well be due to steric inhibition of approach of the nucleophile or departure of the leaving group. The Cl−C−Cl angle at the reaction center is somewhat compressed in the perp transition states. The difference between the most stable allyl chloride substrate conformer (staggered) and its eclipsed form is 1.45 kcal/mol, the eclipsed form having one $i\nu$ = 136 cm^{-1}. [d]This is ΔH for formation of the symmetrical intermediate from substrate plus ammonia. [e]This transition state did not complete; see the Discussion.

triafulvenyl groups.[19−22] It is noteworthy that although the activation enthalpies for reactions of allyl and propyl chlorides pass through "perp" transition states, those in which a 90° rotation about the C_α−C_β bond has occurred from the optimal tss, the *differences* in $\Delta H^{\ddagger}$ are virtually the same for the two 3-carbon systems, optimized and "perp". Hence the importance of π-conjugative alignment in the allylic system is not demonstrated by this result.

The importance of π conjugation between the reaction center and the unsaturated alkyl moiety has been questioned in recent years. Several studies indicate that electrostatic effects are the primary source of activation for benzylic and allylic halides.[23−25] Two very recent papers by Galabov, Allen, et al. describe rigorous quantum mechanical studies on the sources of allylic activation in S_N2 chemistry. We call attention to the fact that in these studies only negatively charged nucleophiles and neutral substrates were used leading to negatively charged transition states,[26a,b] a point we will return to below. The authors conclude that attractive electrostatic interactions in the tss between both the negative nucleophile and leaving group with C_β are the main sources of activation for allylic and benzylic substrates. Therefore, we computed NPA (natural population analysis) charges on the substrates and transition states in Table 2 at the MP2/6-311+G** level, and these are given in Table 3. The reactant state charges at C_α are all similar and small, ranging from 0.028 (allyl chloride) to 0.068 (6-methyl-5,6-dihydrofulvenyl chloride). Positive charge *increases* occur at C_α for all the transition states and range from 0.189 (fulvenyl) to 0.311 (triafulvenyl). The change in positivity at the reaction center is actually 0.030 greater for the propyl system than for allyl, Additionally, charge at C_β becomes more positive (or less negative) in the tss compared to the substrates, especially for the allylic compounds, in agreement with the

Table 3. NPA Charges on Alkyl Chlorides and Alkylammonium Ions and Their Identity S_N2 Substitution Reaction Transition States[a]

alkyl group	C_α	C_β	C_γ (or ring)	LG[b]
chlorides				
allyl	0.028	−0.011	0.026	−0.044
ts	0.221	−0.001	−0.008	−0.991[b]
propyl	0.043	−0.007	0.022	−0.059
ts	0.266	−0.022	0.014	−0.990
benzyl	0.060	−0.074	−0.007	−0.054
ts	0.241	−0.064	−0.113	−0.929[b]
fulvenyl	0.036	0.112	−0.106	−0.042
ts	0.189	0.157	−0.263	−0.893[b]
5,6-dihydrofulvenyl	0.057	0.039	−0.037	−0.059
ts	0.257	0.026	0.097	−1.380[b]
6-methylfulvenyl	0.049	0.079	−0.082	−0.046
ts	0.204	0.145	−0.259	−0.886[b]
6-methyl-5,6-dihydrofulvenyl	0.068	−0.019	0.012	−0.061
ts	0.279	−0.051	−0.007	−0.942[b]
triafulvenyl	0.046	−0.142	0.188	−0.092
ts	0.311	0.189	0.024	−1.524[b]
3,4-dihydrotriafulvenyl	0.058	−0.010	0.022	−0.070
ts	0.270	−0.029	0.148	−1.389[b]
ammonium ions				
allyl	0.256	−0.056	0.151	0.649
ts	0.348	−0.053	0.130	0.922[b]
propyl	0.272	−0.001	0.080	0.650
ts	0.372	−0.002	0.055	0.946
fulvenyl	0.259	0.063	0.027	0.652
ts	0.351	0.033	0.039	0.930[b]
5,6-dihydrofulvenyl	0.281	0.064	0.007	0.647
ts	0.371	0.031	0.013	0.955[b]
triafulvenyl	0.257	−0.208	0.335	0.616
ts	0.383	−0.157	0.604	0.594[b]
intermediate	0.393	−0.125	0.656	0.469[b]
3,4-dihydrotriafulvenyl	0.276	0.026	0.052	0.646
ts	0.373	−0.010	0.060	0.950[b]

[a]Charges computed at the MP2/6-311+G** level. Charges on hydrogens are summed onto the attached carbons. For the cyclic structures the charge on the entire ring, phenyl, 5-membered, or 3-membered, are listed. [b]These are the charges on the entire reaction center: LG−CH_2−LG. LG = leaving group/nucleophile.

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Table 4. Selected Geometric Features of the Alkyl Chlorides, Alkylammonium Ions, and Their Identity S_N2 Substitution Transition States (Distances in Angstroms)[a]

alkyl group	d(C_α–C_β)	d(C_β–C_γ)	Δd(C_α–C_β)[b]	Δd(C_α–C_β)[b]	d(C_β–LG)[c]	avg *d* (ring)[d]
			chlorides			
allyl	1.501	1.339			1.780	NA
ts	1.464	1.344	−0.037	0.005	2.340	NA
propyl	1.519	1.529			1.787	NA
ts	1.507	1.524	−0.012	−0.005	2.341	NA
benzyl	1.498	1.403			1.798	1.400 ± 0.002
ts	1.468	1.403	−0.030	0	2.322	1.400 ± 0.003
fulvenyl	1.488	1.357			1.795	1.428 ± 0.050
ts	1.455	1.368	−0.033	0.011	2.302	1.424 ± 0.034
5,6-dihydrofulvenyl	1.520	1.536			1.789	1.439 ± 0.072
ts	1.510	1.535	−0.010	0.011	2.319, 2.341	1.438 ± 0.062
6-methylfulvenyl	1.497	1.365			1.798	1.428 ± 0.049
ts	1.464	1.374	−0.033	0.009	2.291, 2.319	1.424 ± 0.038
6-methyl-5,6-dihydrofulvenyl	1.525	1.545			1.792	1.439 ± 0.064
ts	1.516	1.547	−0.009	0.002	2.342, 2.343	1.438 ± 0.063
triafulvenyl	1.484	1.339			1.816	1.408 ± 0.050
ts	1.431	1.342	−0.053	0.003	2.452	1.406 ± 0.046
3,4-dihydrotriafulvenyl	1.519	1.517			1.792	1.446 ± 0.092
ts	1.509	1.513	−0.010	−0.004		1.445 ± 0.050
acetonyl[e]	1.523	1.504			1.781	NA
acetonyl ts[e]	1.495	1.508	−0.028	0.004	2.295	NA
			ammonium ions			
allyl	1.495	1.342			1.526	NA
ts	1.474	1.345	−0.021	0.003	2.080	NA
propyl	1.520	1.531			1.517	NA
ts	1.515	1.528	−0.005	−0.003	2.059, 2.060	NA
fulvenyl	1.502	1.357			1.523	1.430 ± 0.055
ts	1.466	1.360	−0.036	0.003	2.085, 2.091	1.430 ± 0.053
5,6-dihydrofulvenyl	1.521	1.539			1.517	1.440 ± 0.067
ts	1.516	1.530	−0.005	−0.009	2.041, 2.069	1.441 ± 0.066
triafulvenyl	1.350	1.478			1.547	1.400 ± 0.043
ts	1.385	1.385	0.035	−0.093	2.238, 2.978	1.389 ± 0.025
intermediate	1.363	1.404	0.013	−0.074	2.814, 2.814	1.384 ± 0.019
3,4-dihydrotriafulvenyl	1.522	1.527			1.515	1.446 ± 0.097
ts	1.517	1.521	−0.005	−0.006	2.054, 2.061	1.445 ± 0.091

[a]Calculated at the MP2/6-311+G** level. [b]Distance in transition state minus that in substrate. [c]The two C–Cl distances in the transition states are the same. [d]Average C–C distances in the phenyl ring (benzyl) or the 5-membered ring (fulvenyl/5,6-dihydrofulvenyl) or the 3-membered ring (triafulvenyl-3,4-dihydrotriafulvenyl). [e]These distances were obtained at the G3MP2 level.

Galibov–Allen–Wu (GAW) model.[26b] If conjugative π delocalization is significant then, as Streitwieser suggests, the C_α–C_β bond should become shorter in the transition states.[25] This in fact does occur for all reactions, but only by 0.05 Å or less, at least for the reactions of the nonallylic substrates; see Table 4. We conclude that for these all-hydrocarbon R groups the reactant-state polarity is of less importance than it is in such highly activated polar systems as acetonyl chloride and cyanomethyl chloride (and more modestly expressed by *para*-substituted benzyl halides),[26a] but that transition-state polarity is critical.

The differences between calculated activation enthalpies for the allylic substrates, and their nonallylic, dihydro analogues are in line with the known experimental reactivity increases as mentioned above. All the allylic substrates are more reactive by experiment and by calculation than their dihydro analogues except for triafulvenyl, which is calculated to be *less* reactive than its dihydrotriafulvenyl analogue. The reactivity increase is especially marked for the fulvenyl substrate. The GAW (Galibov–Allen–Wu) model[26b] seems to handle the reactions of the alkyl chlorides with chloride, but with a slight modification to account for the reactivity of the fulvenyl substrate. Thus, we propose that in the S_N2 transition state for allylic halides the positive charge at C_β leads to electrostatic compensation at C_γ (including its ring if applicable) which becomes more negative. This increase in negativity is in fact seen for the transition states of allyl and benzyl substrates, but is especially notable for the fulvenyl ts. The exception again is for the reaction of the triafulvene substrate where the ring remains positive although less so than in the substrate. Nonallylic substrates experience little change or a slight increase in *positivity* at C_γ in the ts. The fulvenyl transition state is best able to increase its negativity at C_γ because it can become somewhat cyclopentadienide-like, exhibiting a π response within the five-membered ring to the demand made by the charge at C_β. The triafulvenyl transition state is least able to respond in this fashion since this would require a contribution from an antiaromatic cyclopropenide fragment. This conclusion is reinforced by the reduction of bond length alternation shown in the 5-membered ring of the fulvenyl

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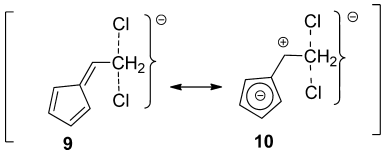
transition state compared with the other transition states. Again, the phenyl ring in the benzyl system is different as it preserves its benzenoid geometry; see Table 4.

An alternate, somewhat simpler statement of the effect of the fulvenyl group on the stability of the S_N2 transition state in the chloride reaction notes that the overall charge on these transition states is −1 (Scheme 4). Most of the negative charge

Scheme 4. Stabilization from Cyclopentadienide Resonance Form

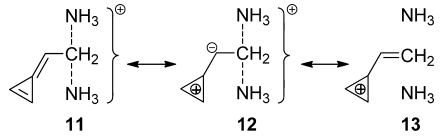


is borne by the chlorines, but the amount of negative charge on the chlorines is less in the fulvenyl and 6-methylfulvenyl transition states than in their dihydro analogues: by 0.138 for fulvenyl and by 0.131 for 6-methylfulvenyl. The rest of the negativity is, of course, carried by the fulvenyl moieties, not possible for the dihydro analogues. This viewpoint, not a contradiction of the more detailed GAW model, has the advantage of direct application to the acidities of alcohols and carboxylic acids bearing the fulvenyl group, where the same reasoning can be applied to their conjugate bases; see the discussion below.

Alkylammonium Ions. The importance of overall transition-state charge was investigated using identity S_N2 reactions of several primary alkylammonium ions, namely allylammonium$^+$, 6-(ammoniomethyl)fulvene$^+$, 4-(ammoniomethyl)triafulvene$^+$, 9-(ammoniomethyl)heptafulvene$^+$, and their nonallylic dihydro analogues. The calculated activation enthalpies are also found in Table 2, the npa charges in Table 3, and selected bond lengths in Table 4. The results show that once again the allyl and fulvenyl groups activate the reaction relative to their dihydro, nonallyic analogues. Since π-electron resonance linking the fulvenyl group with the positive reaction center in the transition state would produce antiaromatic cyclopentadienyl$^+$ character in the five-membered ring, it does not occur. Rather, the Streitwieser electrostatic polarization model in which the unsaturated C_α−C_β bond offers some stabilization of the transition state provides a satisfactory conceptual framework.[25]

In stark contrast, the 4-ammoniotriafulvenyl ion shows a dramatic increase in reactivity relative to its dihydro analogue: $\Delta\Delta H^\ddagger$ is almost 17 kcal/mol at the G3MP2 level and at MP2/6-311+G**! Additionally, the two C_α−N distances are unequal and unusually long at 2.238 and 2.978 Å compared with the other ammonium ion transition states listed in Table 4. As well, the positive charge on the N−C−N reaction center is much reduced relative to the other transition states, the difference having been transferred to the three-membered ring; see Table 3. These results strongly imply a special role for the unsaturated triafulvene moiety. We postulate that in this case a direct π donation from the triafulvene group to the highly positive reaction center stabilizes the transition state; see Scheme 5. The differences between the transition states in the alkyl halide systems and the alkylammonium ion systems may be expressed by imagining that the former resembles the usual conception of an S_N2 transition state while the latter has considerable S_N1 character. In fact, the triafulvenyl ts, though bimolecular, can

Scheme 5. Stabilization from Cyclopropenyl Cation Cesonance form



also be imagined as an S_N1 transition state with backside solvation from a second ammonia molecule.

The great asymmetry of the calculated triafulvenyl ts with respect to its C_α−N bond distances is surprising for an identity S_N2 transition state. In addition, the ts structure was very sensitive to the optimization level (MP2/6-31G* from the G3MP2 calculation vs MP2/6-311+G**), suggesting a very flat energy surface. Therefore, we searched for a more symmetrical structure. A structure with C_s symmetry and equal C_α−N bond distances (2.814 Å) was found, an IRC calculation showing that it is connected to the transition state. The symmetrical structure turns out to be a stable intermediate, its enthalpy lying 0.7 kcal/mol lower than that of the two asymmetric, enantiomeric transition states which flank it on a relatively flat energy surface. Figure 2 shows this relationship. Like the ts, the

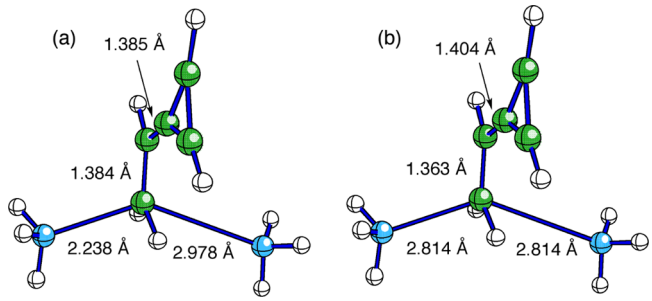


Figure 2. Transition state (a) and the symmetrical intermediate (b) for the identity substitution reaction of 4-ammoniomethyltrifulvene$^+$ with ammonia. Geometries at the MP2/6-311+G** level.

intermediate has considerable positive charge in the three-membered ring, this ring having even more similar C−C distances (average = 1.384 ± 0.019 Å) than does the ts.

We also attempted to calculate a transition state for the 9-(ammoniomethyl)heptafulvenyl ion, thinking that it would be similar to that for the triafulvenyl ion. However, the optimization did not converge, instead trending toward the product of the identity substitution reaction. We propose that the ts for this reaction is an "exploded", highly S_N1-like structure, and that the S_N2 ts is in fact avoided as "not competent". It seems likely that an attempt to synthesize 9-(ammoniomethyl)heptafulvene$^+$ would result in a heptafulvenyl carbocation, a scenario reminiscent of Doering and Knox's original synthesis of tropylium bromide.[27] In support of this speculation, treatment of 7-*N*,*N*-dimethylamino-1,3,5-cycloheptatriene with dilute perchloric acid "immediately" produces the UV spectrum of tropylium ion.

The charge distributions within the 6-(chloromethyl)fulvene ts and the 4-(ammoniomethyl)triafulvene ts are interesting in that both show charge alternation between C_α (together with the partially bonded nucleophile and nucleofuge), C_β, and C_γ, here taken as the ring. In the chloromethylfulvene ts, the alternation, respectively, is $\delta-$, $\delta+$, $\delta-$, whereas in the (ammoniomethyl)triafulvene ts it takes the opposite order,

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$\delta+$, $\delta-$, $\delta+$. This type of alternating charge distribution is reminiscent of that for transition states in identity proton-transfer reactions between negative bases for which the proton donor, the transferred proton, and the proton acceptor have a "charge triplet" arrangement: $\delta-$, $\delta+$, $\delta-$.[28] The electrostatic stabilization permitted by such distributions is clear, and can be expected for similar processes, especially in the gas phase.

Effect of the Fulvenyl Group on the Acidities of Carboxylic Acids and Alcohols. Additional support for the special effect of the fulvenyl group in stabilizing nearby negative charge comes from experimental measurements and calculations of the acidities of carboxylic acids (Table 5) and alcohols (Table 6) bearing this group (Figure 3). These systems greatly attenuate or eliminate the ability of the stabilizing group to conjugate with the reaction center. If polarization of the π systems rather than conjugation is the key factor in them accelerating S_N2 reactions, then they should have a similar impact on the acidities of these substrates. To support the computational data, the gas-phase acidity of 6-methylfulvene-6-carboxylic acid was measured experimentally via the Cooks kinetic method.[17] The resulting value matches the computed value well within experimental uncertainty. This value and those for the four other species for which experimental values are available also confirm that the G3MP2 method is quantitatively accurate in these systems: ΔH_{ACID} (G3) = 1.003ΔH_{ACID} (exp) − 1.200; r^2 = 0.998.

For the carboxylic acids, the fulvenyl acids **14** and **7** are more acidic than their dihydro analogues **16** and **18** by about 5 kcal/mol. They are also more acidic than benzoic acid, which is isomeric with **14** and also has six π electrons in the hydrocarbon portion of the acid. They are also more acidic than acids which do not have the fulvenyl group, namely **20**, **22**, and **24**. The fulvenyl acids are even more acidic than 3,3-difluoroacrylic acid, making the acidifying effect of fulvenyl groups somewhat greater than the 2,2-difluorovinyl group.

Table 5. Calculated (G3MP2) Acid Dissociation Enthalpies (ΔH_{ACID}) for Fulvene-6-carboxylic Acid and Related Acids (kcal/mol)

acid	ΔH_{ACID} (calc)[a]	ΔH_{ACID} (exp)[b]
fulvene-6-carboxylic acid (**14**)	337.5	
6-methylfulvene-6-carboxylic acid (**7**)	335.6	336 ± 3[c]
5,6-dihydrofulvene-6-carboxylic acid (**16**)	342.2	
6-methyl-5,6-dihydrofulvene-6- carboxylic acid (**18**)	341.6	
3-homofulvene-7-carboxylic acid (**20**)	343.2	
triafulvene-4-carboxylic acid (**22**)	352.8	
heptafulvene-8-carboxylic acid (**24**)	342.8	
benzoic acid	340.8	340.1 ± 2.2
1,3-cyclopentadiene	354.2	353.9 ± 2.2
acrylic acid	344.4	344.2 ± 2.9
trans-3-fluoroacrylic acid	339.8	
3,3-difluoroacrylic acid	339.1	

[a]The calculated values are corrected for the enthalpy of the proton at STP. [b]Bartmess, J. E. In *NIST Standard Reference Database Number 69*; Mallard, W. G., Linstrom, P. J., Eds.; National Institute of Standards and Technology: Gaithersburg, MD, 2005 (http://webbook.nist.gov). Bartmess, J. E. In *NIST Standard Reference Database Number 69*; Mallard, W. G., Linstrom, P. J., Eds.; National Institute of Standards and Technology): Gaithersburg, MD, 2005 (http://webbook.nist.gov. [c]This work.

Table 6. Calculated (G3MP2) Acid Dissociation Enthalpies (ΔH_{ACID}) for Fulven-7-ol and Related Alcohols (kcal/mol)

alcohol	ΔH_{ACID} (calc)[a]	ΔH_{ACID} (exp)[b]
fulven-7-ol (**15**)	363.6	
6-methylfulven-7-ol (**4**)	364.7	
5,6-dihydrofulven-7-ol (**17**)	374.5 (324.4)[c]	
6-methyl-5,6-dihydrofulven-7-ol (**19**)	373.0 (341.6)[c]	
heptafulven-9-ol (**21**)	367.3	
triafulven-5-ol (**23**)	382.9	
fulven-6-ol (**25**)	329.3	
cyclopentadiene-5-carboxaldehyde	329.4	
benzyl alcohol	369.8	370.0 ± 2.1

[a]The calculated values are corrected for the enthalpy of the proton at STP. [b]Bartmess, J. E. In *NIST Standard Reference Database Number 69*; Mallard, W. G., Linstrom, P. J., Eds.; National Institute of Standards and Technology: Gaithersburg, MD, 2005 (http://webbook.nist.gov). [c]In these two cases, the more stable alcohol anion results from internal proton transfer from C5 of the 5-membered ring to the oxygen giving a substituted cyclopentadienide anion.

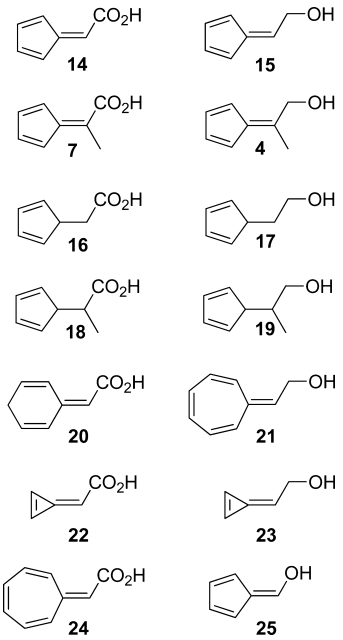

Figure 3. Selected structures of species in Tables 5 and 6.

Acids **22** and **24** are designed to offer stabilization to cations and might have been able to donate electron density toward any center of partial positive charge, but the effect in **24** is minor. Compared with the dihydro acids, the triafulvene acid **22** is in fact quite a bit weaker. Some of this effect might be due to the smaller size and polarizability of the triafulvenyl group, but the acid weakening effect is quite large in **22**, likely a result of the large dipole created by the triafulvene moiety. The effect of the methyl group at C6 of the fulvenyl moiety is seen to be slightly acid strengthening, probably owing to a proximate polarizability effect, modified by variable conformational issues, that is, the distance between the nearer oxygen and the carbon of the methyl group, slightly smaller in the 6-methylfulvenyl case than in the 6-methyldihydrofulvenyl case.

For the alcohols a similar pattern is seen, the fulvenols, **15** and **4**, being more than 8 kcal/mol more acidic than the dihydro analogues, **17**, and **19**. They are also significantly more acidic than benzyl alcohol. The methyl effect in **4** vs **15** is

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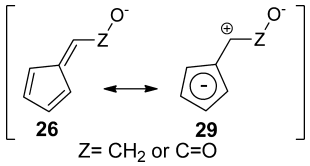
slightly acid weakening, but slightly acid strengthening in **19** vs **17**. In the anion of **4** the negative oxygen is 3.78 Å from the methyl carbon, whereas in the anion of **19** it is 2.86 Å, consistent with a stabilizing polarizability on the anion of **19**, perhaps overridden by a polar effect in the anion of **4**. Heptafulven-9-ol, **21**, though less acidic than fulven-7-ol, is somewhat closer to the latter than in the carboxylic acid set. The greater polarizability in the heptafulvene anion could be partly responsible for this result. An interesting geometric outcome is that the heptafulvene oxyanion has a planar ring whereas that of the alcohol has a pseudoboat conformation. Once again, the triafulvene example is dramatically less acidic than the other species. In the alcohol set, we get another indication of the powerful effect of the cyclopentadienyl moiety in stabilizing anions: over 30 kcal/mol relative to their oxyanion isomers as judged from comparison of the unrearranged and rearranged anion isomers of **17** and **19**.

The anion-stabilizing effect of the fulvenyl group, demonstrated by the data in Tables 5 and 6, is rationalized in the same way as discussed above, namely, that this group is able to help delocalize negative charge by virtue of a contribution from a cyclopentadienide resonance structure (Scheme 6). The

Scheme 6. Stabilization of Conjugate Bases by Cyclopentadienide Resonance Form



magnitude of the effect is slightly larger than observed in the S_N2 processes, which have somewhat more distant and delocalized components in their structures. Overall, it appears that virtually all of the stabilization of the S_N2 pathways having anionic transition states can be accounted for through electrostatic interactions between C_β and the entering and leaving groups and by the polarization of the fulvenyl unit rather than conjugation to the reaction center. This result provides further evidence that the impact of unsaturation adjacent to an S_N2 center is not from conjugation to the reaction center.

Electron-Withdrawing Ability of the Fulvenyl group. Although a direct resonance interaction between the fulvenyl group and the S_N2 reaction center is not supported by the discussion given above, it is of interest to estimate the electron-withdrawing ability, *by resonance*, of fulvenyl and several other strongly attracting, all-hydrocarbon functional groups. To do this, we use acidities as measured by the calculated ΔH_{ACID} values for the R−CH_3 compounds shown in Table 7, taking advantage of a previously established relationship between calculated (MP2/6-311+G**) ΔH_{ACID} values[28] and gas-phase substituent constants.[29] The acids considered here are two singlet carbenes and 6-methylfulvene. We compare them with several conventional electron withdrawing groups, as follows. The total electron-withdrawing ability of the groups, R, in Table 7 may be defined by the ΔH_{ACID} values of R−CH_3, where ΔH_{ACID} = −proton affinity (PA) of the conjugate bases. By this measure, the electron-withdrawing group (EWG) order is CH ≥ CCH_3 > fulvenyl. We can then estimate the resonance portion of the electron withdrawing effects in the form of the gas phase resonance substituent constant, σ_{R^-}[29] using an

Table 7. Calculated (MP2/6-311+G) and Experimental ΔH_{ACID} Values (kcal/mol). Calculated Gas-Phase σ_{R^-} Values for the Hydrocarbon Substituents in This Study[a]**

acid, R−CH_3	ΔH_{ACID} (calc)[b]	ΔH_{ACID} (exp)[c]	est σ_{R^-}
^{1}HC−CH_3	330.6		0.58
$^1CH_3C$−CH_3	334.9		0.57
c-C_5H_4=CH−CH_3[d]	346.2		0.52
Ph−CH_3	383.7	382.3	0.29[e]

[a]In the same way a σ_{R^-} value of approximately 1.0 is calculated for the positively charged $^+CHCH_3$ group. [b]The ΔH_{ACID} values are corrected for zero-point vibrational energy differences. [c]Bartmess, J. E. In *NIST Standard Reference Database Number 69*; Mallard, W. G., Linstrom, P. J., Eds.; National Institute of Standards and Technology: Gaithersburg, MD, 2003 (http://webbook.nist.gov). [d]6-Methylfulvene. [e]The experimental value is 0.22; see ref 29.

established three-parameter correlation obtained for ΔH_{ACID} values obtained in earlier work,[28] given here as eq 1, and in which the resonance effect, ρ_{R^-} = 143.2, is seen to be dominant.

$$\Delta H_{ACID} = -40.2\sigma_F - 143.2\sigma_{R^-} - 20.2\sigma_\alpha + 408.8$$
$$r^2 = 0.987,\ n = 10 \qquad (1)$$

With three substituent constants as the unknowns, three such correlations would be needed. A simpler approach is to approximate two of the three constants, σ_F and σ_α, and thereby estimate σ_{R^-}. For the carbene substituents σ_F was taken as 0.00, the value for ordinary alkyl groups. Using methyl as a guide for CH and ethyl for CCH_3 we approximate σ_α as −0.30 for CH and −0.40 for CCH_3. The exact figures are of little consequence because ρ_α is small. The results give σ_{R^-} = 0.56 for CH ("carbeno") and 0.60 for CCH_3 ("methylcarbeno"). Using the σ values cited, the resonance contribution to the total substituent effect is approximately 93% for CH and 91% for CCH_3. The conclusion is that σ_{R^-} is about 0.6 for the carbeno groups, an unusually large resonance constant.

For the fulvenyl group σ_F was taken as 0.06, the value for the vinyl group, and σ_α as −0.70, the value for the benzyl group, similar in size to the fulvenyl group. This leads to σ_{R^-} = 0.52, another strikingly large value, very like those for the valence-electron deficient "carbeno" groups. Because the resonance sensitivity parameter, ρ_{R^-}, is the major part of the substituent effect (82% using the σ values quoted here) small errors in the assumed polar and polarizability substituent constants once again have little effect on the calculation of σ_{R^-}. For comparison, the relevant data for toluene are also listed. Agreement between the calculated σ_{R^-} value for the phenyl group and that provided by Taft et al.[29] is satisfactory for our purpose.

The σ_{R^-} values listed in Table 7 provide a useful estimate of the strong resonance electron-withdrawing abilities of these unusual but potent hydrocarbon substituents. The size of these effects is remarkable. For comparison the σ_{R^-} values for CHO, NO_2, and NO groups, commonly taken as strong electron-withdrawing groups by resonance, are 0.19, 0.18, and 0.26, respectively.[29]

Summary. In this paper, we show that the diverse reactivity of compounds carrying the fulvenyl group extends to S_N2 substitution reactions at C7, the second carbon from the ring, herein labeled C_α. The fulvenyl group joins other allylic groups in accelerating this reaction relative to dihydro, nonallylic analogues, and in fact increases such reactivity compared with benzyl and allyl substrates. Computational work establishes the

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source of activation in the identity substitution of chloride for chloride as an attractive electrostatic effect between the chlorides and $\delta+$ C_β in the transition state, in agreement with the Galabov–Allen–Wu (GAW) model,[26b] and by further electrostatic aid from the fulvenyl ring which contributes a measure of cyclopentadienide$^-$ character to the ts, creating a stabilizing "ion-triplet" charge distribution. The anion-stabilizing effect of the fulvenyl group is also shown by the acidities of fulvenyl-6-carboxylic acids and fulvenyl-7-ols. Electrostatic delocalization of negative charge in the conjugate base anions by the fulvenyl group is responsible for enhancing these acidities.

An investigation of the positively charged transition states in the identity substitution reactions of ammonia for ammonia reveals an unusual and dramatic activating effect of the triafulvene group. In this case, a direct conjugative interaction of the triafulvenyl group in which the three-membered ring has significant cyclopropenyl$^+$ character provides stabilization of the ts. In fact, the calculated transition state for this reaction is quite loose, with much S_N1 character. In S_N2 ammonia-for-ammonia exchanges of other allylic substrates Streitwieser's electrostatic polarization model[25] gives a good account of the extra reactivity of these compounds.

EXPERIMENTAL SECTION

General Methods. ^{1}H and ^{13}C NMR spectra were recorded on a 500 MHz NMR spectrometer using $CDCl_3$ as solvent and TMS as internal standard, unless specified otherwise. Most column chromatographic separations were carried out on a flash chromatography system using 40–60 mm silica gel columns using ethyl acetate/*n*-hexane solvent mixtures. For preparative TLC, silica gel (grade 60 PF_{254}) was used. All reactions were conducted under an atmosphere of dry nitrogen or argon. Nondeuterated solvents were dried and distilled prior to use. Pyrrolidine is an exceptionally foul-smelling and toxic compound and should be handled with care in a well-ventilated hood. Fulvenes are oxygen- and heat-sensitive compounds; all reactions should be carried out under a nitrogen or argon atmosphere. Exact masses of all new products were verified by high-resolution mass spectra (HRMS). Gas-phase proton affinity measurements were completed in the usual way[17] in a quadrupole ion-trap mass spectrometer with an electrospray ionization source. Ions were generated from approximately a 1:1 mix of the target acid and the reference acid ($\sim 10^{-5}$ M) in methanol. Using the negative-ion mode, the proton-bound complex of the appropriate conjugate bases was isolated and subjected to CID. The CID energy was varied to give spectra with varying extents of fragmentation. The product ratios did not show any significant dependence on the CID energy.

Computational Methods. Structures were built and optimized at lower levels using the MacSpartan Plus software package[30] then optimized at the G3MP2 and, in some cases, the MP2/6-311+G** levels using the Gaussian 03 quantum mechanical programs.[31] All structures reported here represent electronic energy minima, and all structures identified as transition states (tss) have one imaginary frequency, corresponding to the reaction coordinate for the reaction event.

***N*-Benzylamino-6-methylfulvene (2d).** To a solution of 0.35 g (2.5 mmol) of **1** in 10 mL of ethanol was added 0.54 g (5 mmol) of benzylamine, and the mixture was stirred overnight at room temperature. The solution was diluted with 25 mL of H_2O and extracted with 3 × 20 mL portions of diethyl ether. The combined organic layers were washed with brine and dried over $MgSO_4$, and the solvent was rotovapped. The residue was purified by preparative TLC (30% EtOAc–petroleum ether) to give 338 mg (64%) of a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25–7.40 (m, 5H); 6.57 (m, 2H); 6.50 (m, 2H); 3.80 (s, 2H); 3.69 (s, 2H); 2.32 (s, 3H); 1.62 (br S, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 151.0; 141.0, 132.5; 131.9; 129.1; 128.8; 127.8; 121.8; 120.8; 54.0; 53.5; 20.3 ppm. HRMS: calcd for $C_{15}H_{17}N$ 211.1361, found 211.1354.

2-(Cyclopenta-2,4-dien-1-ylidene)propyl Nitrate (5). 6-(Chloromethyl)-6-methylfulvene (**1**) (0.281 g, 2 mmol) was added to a solution (0.374 g, 2.2 mmol) of $AgNO_3$ in 7.5 mL of acetone and 2.5 mL of H_2O. After the solution was stirred for 3 h at room temperature, no reaction was detected by TLC analysis. After being refluxed for 2.5 h, the mixture was cooled to room temperature. The mixture was filtered by gravity, and the filter paper rinsed with ether. The filtrate was transferred to a separatory funnel, the water layer was separated, the organic layer washed once with 10 mL of brine and dried over anhydrous Na_2SO_4, and the solvent was rotovapped. The residue was purified by flash chromatography on silica gel eluting with petroleum ether to give 12 mg (5% yield) of a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.54 (m, 2H); 6.48 (m, 2H); 5.3 (s, 2H); 2.2 (s, 3H). ^{13}C NMR (75 Hz, $CDCl_3$): δ 147.1; 138.8; 134.6; 134.0; 121.9; 120.6; 74.5; 19.3 ppm. HRMS: calcd for $C_8H_9NO_3$ 167.0582, found 167.0612.

Synthesis of 2-(Cyclopenta-2,4-dien-1-ylidene)propanoate (8). To a solution of pyruvic acid (0.35 mL, 5.0 mmol) and cyclopentadiene (0.67 mL, 7.5 mmol) in MeOH (10 mL) was added pyrrolidine (0.92 mL, 11.0 mmol) at 0 °C under a nitrogen atmosphere. The mixture was stirred for 2 h at 25 °C. After removal of the solvent under reduced pressure, the residue, a red oil, was washed with diethyl ether (4 × 10 mL) to remove neutral organic material and dried under high vacuum for 10 min. The product was obtained as a red oil (0.84 g, 4.1 mmol, 82%) (in addition to the pyrrolidinium salt of carboxylate **8**, the ^{1}H NMR contains excess $C_4H_{10}N^+$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.8 (br s, 1H); 6.57 (d, J = 5.0 Hz, 1H); 6.45 (dd, J = 5.0 Hz, 2H); 6.37 (d, J = 5.0 Hz, 1H); 3.1 (m, 4H); 2.32 (s, 3H); 1.87 (m, 4H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.2, 147.5, 141.9, 132.4, 131.2, 123.6, 121.6, 45.0, 24.8, 19.1 ppm. HRMS: calcd for $C_8H_7O_2^-$ 135.0452, found 135.0441.

General Procedure for the S_N2 Kinetics of Benzyl Chloride and 1. For the determination of the pseudo-first-order rate constants, the kinetic runs were conducted in an NMR tube in acetone-d_6 solutions of 0.2 M of substrate (benzyl chloride or **1**) and 0.01 M KI at ca. 23 °C. The progress of the reaction in each case was determined by NMR integrations of the corresponding chloromethyl and iodomethyl resonances. These were observed at 4.72 and 4.62 ppm for the benzyl halide system and at 4.60 and 4.58 ppm, respectively, for the fulvenyl system. Excellent pseudo-first-order plots were obtained in each case. The S_N2 rates were determined by the formula $k(S_N2) = k(S_N1)/0.2$.

ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra for all new compounds, pseudo-first-order plots for **1** and benzyl chloride, full ref 31; Tables S1–S4 contain calculated enthalpies and free energies (G3MP2), electronic energies (MP2/6-311+G**), and zero-point vibrational energies (HF/6-311+G**) for compounds in this study. Imaginary frequencies for transition states (Table S1). Cartesian coordinates for these compounds (Table S5). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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DEDICATION

Dedicated to Professor Armin de Meijere on the occasion of his 75th birthday.

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