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ADDITIONS OF SUBSTITUTED PHENYLTHIYL RADICALS TO SUBSTITUTED α-METHYLSTYRENES

GROUND STATE AND TRANSITION STATE ELECTRONIC EFFECTS[1]

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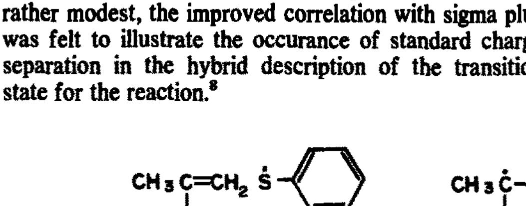
Abstract—The radical addition of substituted thiophenols to α-methylstyrene and substituted α-methylstyrenes has been investigated at 70°. Relative reactivities of pairs of thiophenols competing with individual alkenes can be utilized to obtain Hammett correlations. The interplay of substituent effects in alkene and thiyl radical leads to examples of non-linear rho values. Rationales for this behavior will be offered in terms of variable contributions from ground state and transition state electronic factors as well as in terms of possible mechanistic changes.

The anti-Markovnikoff additions of thiols to alkenes were first observed over seventy years ago.[2] This reaction is now recognized to be a radical process and has been extensively investigated and reviewed both as a specific topic[3] and within the general framework of radical additions.[4]

Substituent effects have been infrequently investigated. Early results from Walling's[5] and Cadogan's[6] groups showed generally negative rho values, for radical addition of thioglycolic acid derivatives to α-methylstyrenes. Later, results on the reaction between these alkenes and phenylthiyl radical (eqn 1) have been reported.[7] An optimum relationship was obtained using sigma plus parameters. Although the magnitude of rho was rather modest, the improved correlation with sigma plus was felt to illustrate the occurance of standard charge separation in the hybrid description of the transition state for the reaction.[8]



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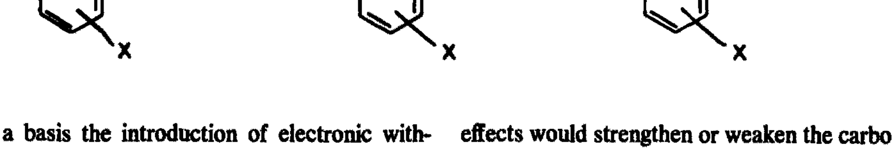


On such a basis the introduction of electronic withdrawing groups in the thiyl radical should also favor the reaction. To verify this, a study of the competitive addition of a series of substituted thiophenols to p-chloro-α-methylstyrene was undertaken.[9] This particular α-methylstryrene was chosen because of its ease of glc separation from the thiol pairs examined. At this time, it was naively felt that the nature of the alkene substituent would only modestly affect the results. A good linear correlation was again found. However, to our surprise, the rho value was negative. Optimum correlation was again with sigma substituent parameters.

The above result cannot easily be reconciled with the typical picture of a partially charge separated transition state in the addition step. One argument which could be advanced to explain these results is that charge separation in the chain transfer step (hydrogen abstraction from the thiols) is being observed. Such a reaction might well exhibit a negative rho value. The reaction of 1-cyano-1-cyclohexyl radical with substituted benzenethiols, for example, has a rho value of −0.52.[10] Despite such analogies, however, it is difficult to see how a similar process could explain the present findings. Probable charge separation in above case suggest that the introduction of electron donating groups in the abstracting radical would retard the observed rate of thiol addition. Our own[7] and prior work,[5,6] as already pointed out show just opposite.

Even more fundamentally, the reality of charge separation in transition states leading to benzylic radicals by hydrogen atom abstraction has been seriously questioned by Zavitsas *et al.*[11] The argument put forward by this group is that those substituent effects which hitherto had been rationalized in terms of a partially charge separated transition state actually could be explained by inductive effects operating in the ground state. Such effects would strengthen or weaken the carbon–hydrogen bond to be broken. Although Zavitsas' initial argument on the unimportance of transition state charge separation and the compensating increased importance of ground state factors was based on H atom abstractions, similar arguments can be put forward for analogous radical additions or perester decompositions.[12] A consequence of the original reasoning was that all benzylic H atom abstractions would exhibit negative rho values. Later work by Pryor[13,14] and Henderson[14] have shown that such H atom abstractions, if carried out by "nucleophilic" alkyl radicals, have positive rho values.

Zavitsas' approach should not, however, be entirely discarded. Recently, Pryor has suggested that both transition and ground state electronic factors should be considered in evaluating substituent effects in radical reactions.[15] The relative importance of these factors may themselves be a function of substituent. Several systems were named where this might be true. Our prior work was one such case. An additional system has also been reported.[16] This suggestion itself is not inherently novel. It must be admitted, however, that many, if not most, of the articles dealing with substituent effects in radical reactions adopt an either/or attitude in regard to ground state versus transition state explanations. The need to consider both factors should be particularly necessary for less endothermic processes.

With the above factors in mind, it was decided to reinvestigate the effects of introducing substituents in thiols on their relative rates of radical addition to alkenes. In the present study, however, a wide range of substituted α-methylstyrene substrates was utilized. Standard procedure is given in the Experimental. Standard comparative kinetic techniques were utilized.[17] All studies were carried out in replicate in nitrogen atmosphere at 70°. Reactions were thermally initiated. Reaction times varied from 35 to 60 min with total thiol consumption varying from 20 to 40%.

The relative rate constants are given in Table 1. Certain data could not be obtained due to either a lack of glc separability or limited solubility of starting materials. Table 2 contains the rho values for thiol substituent variation for each alkene substrate. Although all correlations were optimal when sigma plus constants were utilized, correlations based upon sigma are also given.

The rho values in Table 2 were calculated by linear least square analysis of the relative rate data. While all are rather modest, it was felt that the differences among the more reliable values are real and may be discussed. Correlation coefficients would indicate that greater reliance be placed on the linearity of rho values determined for α-methylstyrene, p-chloro-α-methylstyrene and m-trifluoromethyl-α-methylstyrene. This criterion could, however, be challenged. It has been suggested by Davis and Pryor that the standard deviation from the regression be used as a measure of "goodness of fit" of Hammett correlations.[18] These terms are also given in Table 2.

The correlations for α-methylstyrene and α-methylstyrenes containing electron withdrawing groups are reasonably good using either correlation coefficients, average deviation or standard deviation of the regression as guides. A trend is apparent for these three systems with the greatest selectivity being shown for addition to m-trifluoromethyl-α-methylstyrene. This may be explicable on the basis of ground state considerations. Electrophilic thiyl radicals should be reluctant to attack at sites of low electron density. When a strong electron withdrawing group is present in the aromatic portion of the alkene, the electron density at the reactive double bond is minimized. Such a system should show the greatest selectivity in competitive reaction with thiyl radical. These phenylthiyl radicals which contain electron donating groups will have their electrophilic character internally ameliorated and will be most prone to react at such bonds. As the functional group(s) in the aromatic portion of the alkene become less electron demanding, the exocyclic double bond shown less discrimination in the competitive process. This rationalization would maintain the traditional view than the generation of the benzylic radical in the addition step is rate determining

Table 1. Relative rates of substituted thiyl radical addition to various α-methylstyrenes at 70°

Alkene Substituents	k_X/k_H					
	p-CH$_3$O	*p*-CH$_3$	H	*p*-Cl	*m*-CF$_3$	*p*-NO$_2$
p-CH$_3$O	1.54±0.17	1.25±0.07	1.00	1.35±0.10	1.21±0.03	--
p-CH$_3$	1.90±0.05	1.13±0.05	1.00	1.35±0.03	1.12±0.05	--
H	1.27±0.13	1.11±0.02	1.00	0.99±0.05	--	0.67±0.08
p-Cl	1.65±0.09	1.00±0.02	1.00	0.87±0.08	0.81±0.03	0.54±0.05
m-CF$_3$	1.88±0.18	1.35±0.07	1.00	0.76±0.08	0.58±0.03	--

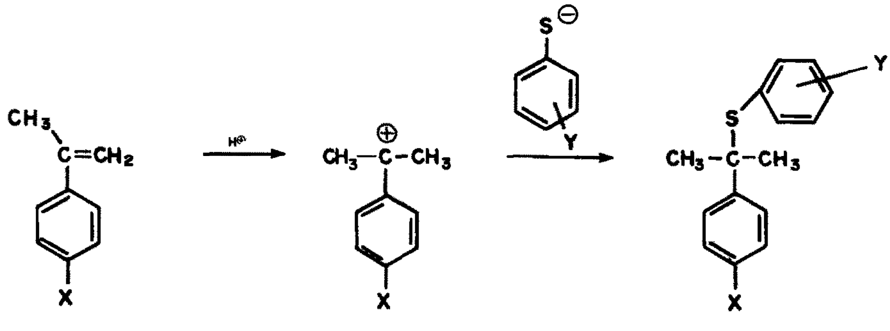
Table 2. Effects of alkene substituents on rho values for substituted thiyl radical addition to various α-methylstyrenes at 70°

Alkene Substituent	Sigma Plus Correlation			Sigma Correlation		
	Rho	Correlation Coefficient	s_b	Rho	Correlation Coefficient	s_b
m-CF$_3$	-0.41±0.02	-0.99	0.04	-0.69±0.03	-0.98	0.07
p-Cl	-0.27±0.04	-0.96	0.03	-0.37±0.04	-0.93	0.08
H	-0.18±0.02	-0.98	0.02	-0.24±0.02	-0.97	0.03
p-CH$_3$	-0.15±0.07	-0.59	0.09	-0.17±0.08	-0.44	0.20
p-CH$_3$O	-0.08±0.05	-0.56	0.07	-0.08±0.05	-0.31	0.15

rather than H abstraction from the thiol. The results could also be rationalized if H abstraction from the thiol were more likely to become the rate determining step when utilizing electron deficient alkenes. It is interesting to note in this regard that the probable rho value for reversible H abstraction from thiophenol by substituted cumyl radicals is quite close to that observed for substituted phenylthiyl radical addition to *m*-trifluoromethyl-α-methylstyrene.[19,20] It must be pointed out, however, that this situation could arise only if electron withdrawing groups in the alkene accelerated the addition step. Such does not appear to be the case.[5–7]

The α-methylstyrenes containing electron donating groups in the aromatic ring appear, at first glance, to continue this trend. The situation, however is not that simple. While a least squares analysis may be applied to any set of data, it is obvious from the large average deviations in calculated rho values and the poor values of correlation coefficients and standard deviations of the regress, possibly non-linear function is here being dealt with. The departure from linearity is caused principally by the unexpected enhanced relative reactivity of *p*-chlorophenylthiyl and *m*-trifluoromethylphenylthiyl radicals. This enhancement is well ourside of possible experimental errors.

One obvious explanation to the behavior of these particular reaction pairs lies in a consideration of the acid-base properties of the systems. The thiols involved here are the most acidic in the series, while the alkenes are the most likely to accept protons. The enhanced reactivity, therefore, might simply be dismissed as arising from a competitive ionic addition (eqn 2).



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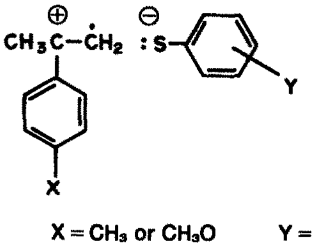
X = CH$_3$ or CH$_3$O Y = *p*-Cl or *m*-CF$_3$

This is apparently not the case. Glc analyses of reaction mixtures showed but a single product. The NMR spectra of reaction mixtures which had gone to completion were consistent with formation of only the anti-Markovnikoff product.

As already pointed out, those particular alkenes are best able to assume a charge separated canonical structure.



X = CH$_3$ or CH$_3$O Y = *p*-Cl or *m*-CF$_3$

Such a contributing form, however, is most compatible when the anionic portion of the system is also electronically stabilized. The above analysis is tantamount to the application of typical charge separated, transition state considerations to a reaction which may be generally controlled by ground state factors. Because the electronic effects in ground state and transition state may independently vary and be due to different factors, e.g. inductive effects vs inductive-mesomeric effects, deviations from linearity need not themselves describe a new linear relation. We feel this provides one example of what may be the general need to treat substitutent effects, especially in relatively exothermic processes, in terms of both ground state and transition state factors.

EXPERIMENTAL

Materials. Reagent benzene and *o*-dichlorobenzene were used without further purification. Commercial α-methylstyrene was distilled before use. In general, the substituted α-methylstyrenes were prepared from the appropriate aryl Grignard and acetone, followed by dehydration, according to literature methods.[21] Thiophenol and most substituted thiophenols were commercially obtained. *m*-Trifluoromethylthiophenol was prepared from *m*-trifluoromethylaniline by diazotization followed by reaction with sodium disulfide. The resulting organic sulfide was reduced to the thiol by treatment with zinc and acetic acid.[22] Glc analysis showed the purity of all compounds to be greater than 98%. Physical properties of all compounds agreed with literature values.

Equipment. All glc analyses were performed on a Varian Aerograph Model 202B and a Sargent recorder with disc integrator. A 0.25 in. × 12 ft aluminum column packed with 5% SE-30 on Chromosorb W or a 0.25 in. × 12 ft aluminum column packed with 8% FFAP on Chromosorb W were used.

Product study. Several reactions between individual alkenes and thiols have been investigated.[7] In all cases, material balances in excess of 90% have been observed. No Markovnikoff adducts were isolated or spectroscopically detected.

Kinetics. Our basic kinetic approach has been previously described.[17] Mixtures of alkene, thiophenol I, thiophenol II, *o*-dichlorobenzene and benzene in approximate ratios of 1:1:1:1:5 were prepared. Samples were degassed by freeze-thaw cycles. Reactions were run in a nitrogen atmosphere at reduced pressure for periods of 35–60 min. Analysis were by glc.

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