Unusual Activation by an Azulenyl Substituent

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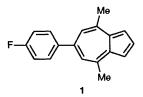
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The methoxydefluorination of 4,8-dimethyl-6-(p-fluorophenyl)azulene proceeds at 1100 times that of fluorobenzene under the same conditions, and reflects the strongly electron withdrawing nature of the seven-membered ring in the azulene system, in contrast with benzenoid and alkyl substituents in S_NAr processes.

Aryl substituents in general are mildly activating towards both electrophilic¹ and nucleophilic^{2,3} reactions of benzene systems.

Perkins⁴ earlier noted that the cyclopentadienyl structure in acenaphthylene considerably accelerated the methoxydehalogenation of 5-chloroacenaphthylene, compared with that of 1-chloronaphthalene. This was ascribed to the stability of the cyclopentadienyl anion structure which was a contributor to the Meisenheimer intermediate from the former compound, and which was not available in the reaction of 1-chloronaphthalene. No kinetic measurement of the acceleration was attempted, however, although a study of the rates of methoxydehalogenation of a number of polyfluorinated polybenzenoid aromatic compounds found that octafluoroacenaphthylene underwent reaction some orders of magnitude more quickly than the corresponding derivatives of biphenyl, phenanthrene, and biphenylene; this was also attributed to the unusual stabilising effect of the five-membered ring system.⁵

We have recently⁶ observed that the methoxydechlorination of some derivatives of 6-chloroazulene proceeded very readily, and ascribed this to the tropylium-like nature of the seven-membered ring to which the halogen is attached. This



explanation carried with it the implication that a 6-azulenyl substituent would have considerable electron-withdrawing properties, and we therefore prepared 4,8-dimethyl-6-(*p*-fluorophenyl)azulene 1 and set about the measurement of its rate of methoxydefluorination. Fluorobenzene itself is nearly inert to methoxide ion (MeOH, 323 K)⁷ although a rate constant for this reaction has been found (k_2 , 4.7 × 10⁻⁷ dm³ mol s⁻¹, 323 K) in dimethyl sulphoxide (DMSO)–MeOH (9:1, v/v).⁸

4,8-Dimethyl-6-(*p*-fluorophenyl)azulene (m.p., 94–5 °C) was prepared from the reaction of cyclopentadienyl sodium with 2,6-dimethyl-4-(*p*-fluorophenyl)pyrylium hydrogen sulphate, itself obtained from *p*-fluorophenylmagnesium bromide and 2,6-dimethyl-4-pyrone through the Grignard synthesis and treatment of the intermediate alcohol with 50% sulphuric acid.^{9,10} Analogously, 4,8-dimethyl-6-(*p*-methoxyphenyl)azulene (m.p., 74–75 °C) was obtained from *p*-methoxyphenylmagnesium bromide. Both compounds showed satisfactory combustion analyses and proton NMR spectra.

When the fluoro-compound was boiled with sodium methoxide $(1 \text{ mol } dm^{-3})$ overnight, the methoxy-compound

could be detected in small amount (TLC). Two measurements of the rate of fluoride-ion displacement from 1 by sodium methoxide in DMSO-MeOH (9:1, v/v, 323 K) showed the second-order rate constant to be $5.1 \pm 0.1 \times 10^{-4}$ dm³ mol⁻¹ s⁻¹ over 60-70% reaction, consistent with an acceleration by the *p*-(4,8-dimethyl-6-azulenyl) substituent by a factor of *ca.* 1.1×10^3 . This is much greater than the acceleration shown by the *p*-phenyl substituent (4.0) and similar to that found for the *m*-halogen substituents.

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