Unusual Activation by an Azulenyl Substituent

Roger Bolton* and Alexandra J. Pilgrim

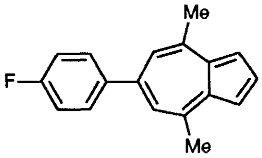
Department of Chemistry, Royal Holloway and Bedford New College, Egham, Surrey TW20 0EX, UK

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 electrophilic[1] and nucleophilic[2,3] reactions of benzene systems.

Perkins[4] 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 recently[6] 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



1

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} dm^3 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 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 $5.1 \pm 0.1 \times 10^{-4}$ dm^3 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.

Received, 4th September 1991; Com. 1/04596B

References

1 P. B. D. de la Mare, *Electrophilic Halogenation*, Cambridge University Press, Cambridge, 1976, p. 67.
2 R. Bolton and J. P. B. Sandall, *J. Fluorine Chem.*, 1978, **12**, 463.
3 J. Miller, *Aromatic Nucleophilic Substitution*, Elsevier, Amsterdam, 1968.
4 M. J. Perkins, *J. Chem. Soc., Chem. Commun.*, 1971, 231.
5 R. K. Atwal and R. Bolton, *Aust. J. Chem.*, 1987, **40**, 241.
6 R. Bolton, D. G. Hamilton and J. P. B. Sandall, *J. Chem. Soc., Chem. Commun.*, 1990, 917; *J. Chem. Soc., Perkin Trans. 2*, 1991, 431.
7 R. Bolton and J. P. B. Sandall, *J. Chem. Soc., Perkin Trans. 2*, 1978, 746.
8 R. Bolton and J. P. B. Sandall, *J. Fluorine Chem.*, 1982, **21**, 459.
9 A. Baeyer and J. Piccard, *Liebig's Ann. Chem.*, 1911, **384**, 208.
10 K. Hafner and H. Kaiser, *Liebig's Ann. Chem.*, 1958, **618**, 140.