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THE 3,5-DICHLORO-4-CYANOPHENYL GROUP. A USEFUL MOIETY FOR THE EXTENSION OF $\rho\sigma^+$ STUDIES.

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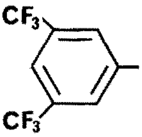
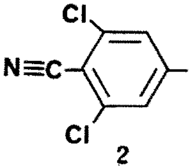
The use of $\rho\sigma$ and $\rho\sigma^+$ studies has been shown to be of great value in the determination of the mechanisms of a wide variety of organic reactions.[3] The recent applications of $\rho\sigma^+$ correlations to the study of neighboring group participation in carbonium ion reactions[4,5] has been limited by the synthetic problems involved in obtaining the precursors for the preparation of benzylic cations where the aryl group is functionalized with strong electron-withdrawing substituents. Since the most common routes to desirable aryl substituted carbinols utilize the addition of organometallic reagents to various carbonyl compounds, the presence of nitro and cyano functions is generally prohibited. Thus, the most strongly electron-withdrawing aryl moiety which is readily available is the 3,5-bis(trifluoromethyl)-phenyl grouping, 1, which has an additive substituent σ^+ of 1.04. The need for an even stronger electron-withdrawing aryl system[5] prompted us to prepare the 3,5-dichloro-4-cyanophenyl grouping, 2. We now wish to report the synthesis,[6] utilization, and the additive substituent σ^+ for this moiety.



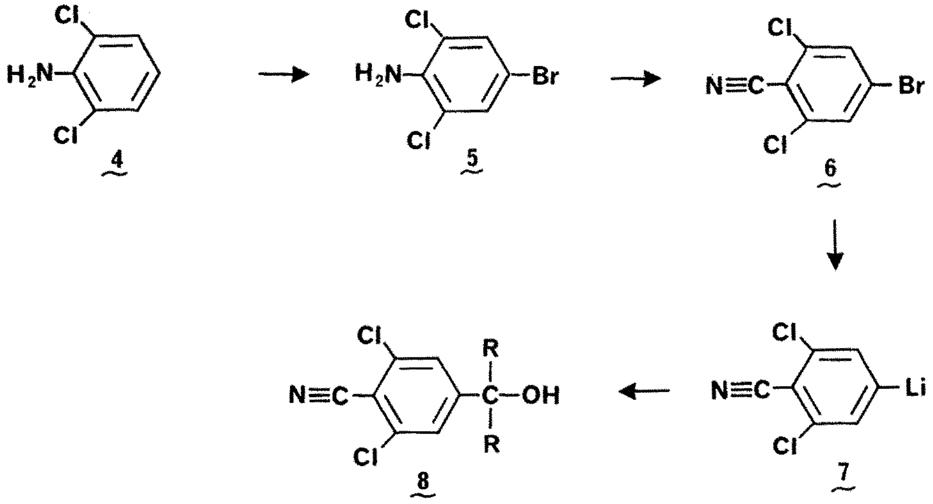
1



2

In order to prepare the necessary organometallic reagents for the subsequent synthesis of carbinols substituted with 2, we required 4-bromo-2,6-dichlorobenzonitrile (3). Starting with commercially available 2,6-dichloroaniline (4), we prepared 4-bromo-2,6-dichloroaniline

(5) in 85% yield according to the published procedure.[7] Diazotization of 5 in an acetic acid-water-sulfuric acid (*ca.* 20:3:5) solution with sodium nitrite at < 15° gave the expected diazonium salt which on reaction with cuprous cyanide at 50° gave 6, m.p. 69-70° (60% yield). Dropwise addition of an ethereal solution of 6 to a solution of n-butyllithium in ether-hexane (*ca.* 3:1) solvent at -70° gave 7. The solution of 7 was maintained at -70° for 5 min. and then an ethereal solution of the appropriate carbonyl compound was added dropwise over a 5 min. period. The reaction mixture was stirred for 5 min. at -70°, allowed to warm to room temperature and hydrolyzed with water. Extraction of the carbinol followed by purification gave 30-40% yields of 8.



Utilizing the procedure outlined above, 2-(3,5-dichloro-4-cyanophenyl)-2-propanol (8, R = CH_3) was obtained in 31% yield. This carbinol was converted into 2-chloro-2-(3,5-dichloro-4-cyanophenyl)propane (9) with anhydrous hydrochloric acid-ferric chloride in methylene chloride. The additive σ^+ of the substituents of 2 was determined by measuring the rate of solvolysis of 9 in 60 wgt.% aqueous acetone according to the procedure of Okamoto and Brown.[8] Since the standard system for the determination of σ^+ constants[9] was the hydrolysis of substituted cumyl chlorides in 90 vol.% aqueous acetone at 25°, we converted our data (Table 1) to the reference conditions using the procedure previously described for such extrapolations.[8]

Table 1

Rates of Hydrolysis of 2-Chloro-2-(3,5-dichloro-4-cyanophenyl)propane

Solvent	Temp. °C	k (sec^{-1})	$\Delta H^{\ddagger}$ (Kcal/mole)	$\Delta S^{\ddagger}$ (e.u.)
60 wgt.% acetone	100.0 ± 0.01	$(2.37 \pm 0.03) \times 10^{-4}$		
	110.0 ± 0.02	$(5.70 \pm 0.08) \times 10^{-4}$		
	120.0 ± 0.02	$(1.26 \pm 0.01) \times 10^{-3}$	23.6	-12.3
	(25.0)[a]	6.15×10^{-8}		
90 vol.% acetone	(25.0)[a]	3.62×10^{-10}		

a) extrapolated rate constants

Using the Hammett equation, $\rho\sigma^{+} = \log \frac{k_X}{k_O}$, with $k_O = 12.4 \times 10^{-5}$ sec^{-1} for the parent cumyl chloride and $\rho = -4.54$,[8,9] we determined the additive σ^{+} of the 3,5-dichloro and 4-cyano substituents to be 1.22.

It is not surprising that the measured value of 1.22 is somewhat lower than the calculated value for σ^{+} of 1.46 ($\sigma_{\underline{p}}^{+}$ for -CN = 0.66 and $\sigma_{\underline{m}}^{+}$ for -Cl = 0.40). The strictly additive relationship breaks down for substituents ortho to each other due to pronounced field effects, steric interactions and most importantly, resonance interactions.

Application of the procedure outlined above for the synthesis of carbinols substituted with the 3,5-dichloro-4-cyanophenyl group will permit significant progress to be made in the study of carbonium ions substituted with aryl groups which are relatively weak carbonium ion stabilizers. The σ^{+} value of 1.22 represents the most positive σ^{+} value which can be easily attained for the general class of aryl substituted carbinols. As such, this moiety provides a sizable extension of the range over which $\rho\sigma^{+}$ correlations of carbonium ion reaction can be made.

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(1) Alfred P. Sloan Foundation Research Fellow, 1967-1969.

(2) Battelle Memorial Institute Staff Fellow, 1967-1969.

(3) For a recent compilation see J. E. Leffler and E. Grunwald, ''Rates and Equilibria of Organic Reactions,'' J. Wiley and Sons, Inc., New York, N. Y., 1963, p. 208.

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