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ELECTRONIC EFFECTS ON CARBON-CHLORINE BONDS[1]

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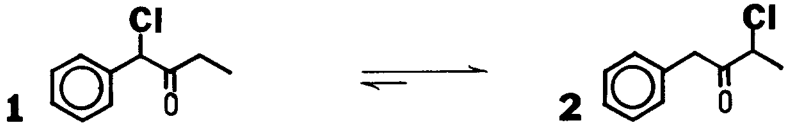
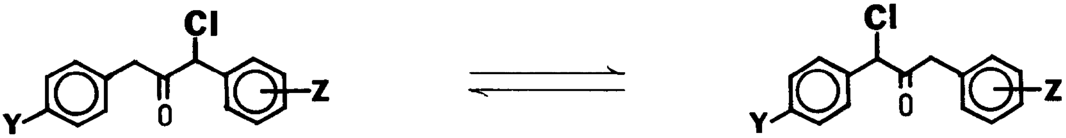
Abstract: For the first time a reaction has been found to study electronic effects on C-Cl bonds in an equilibrium situation. The reaction, the $\alpha \rightleftharpoons \alpha'$ rearrangement of α-chlorodibenzyl ketones, correlates well with the difference in Taft $\sigma°$ values with ρ +0.75.

The acid-catalyzed $\alpha \rightleftharpoons \alpha'$ rearrangement of α-bromo and α-chloro ketones is general.[2] With most α-chloro ketones the reaction occurs by the enol allylic halide mechanism,[2,3] and the equilibration of the α- and α'-isomers is surprisingly clean.[4] This fact suggested the use of the reaction to study structural effects on carbon-chlorine bonds. That the effects could be appreciable was implied by the 10:1 equilibrium ratio for the **2**:**1** pair.[2] The



1.3 kcal./mol. energy difference between the two isomers is unlikely to be mainly steric in origin, and it probably arises mostly from the difference in electronic effect on the C-Cl bond of the methyl sp^3-carbon in **2** relative to the phenyl sp^2-carbon of **1**. However the unsymmetrical nature of the **1** $\rightleftharpoons$ **2** pair made interpretation ambiguous. Therefore, to assess the potential of the rearrangement to measure substituent effects, a series of four substituted dibenzyl ketones **3K** - **6K** was prepared, and their α-chloro derivatives **3-6 A** and **B** were equilibrated.[5] The symmetry of the carbon skeleton guaranteed that any effect on the equilibrium position must be due to the substituents on the aryl rings.



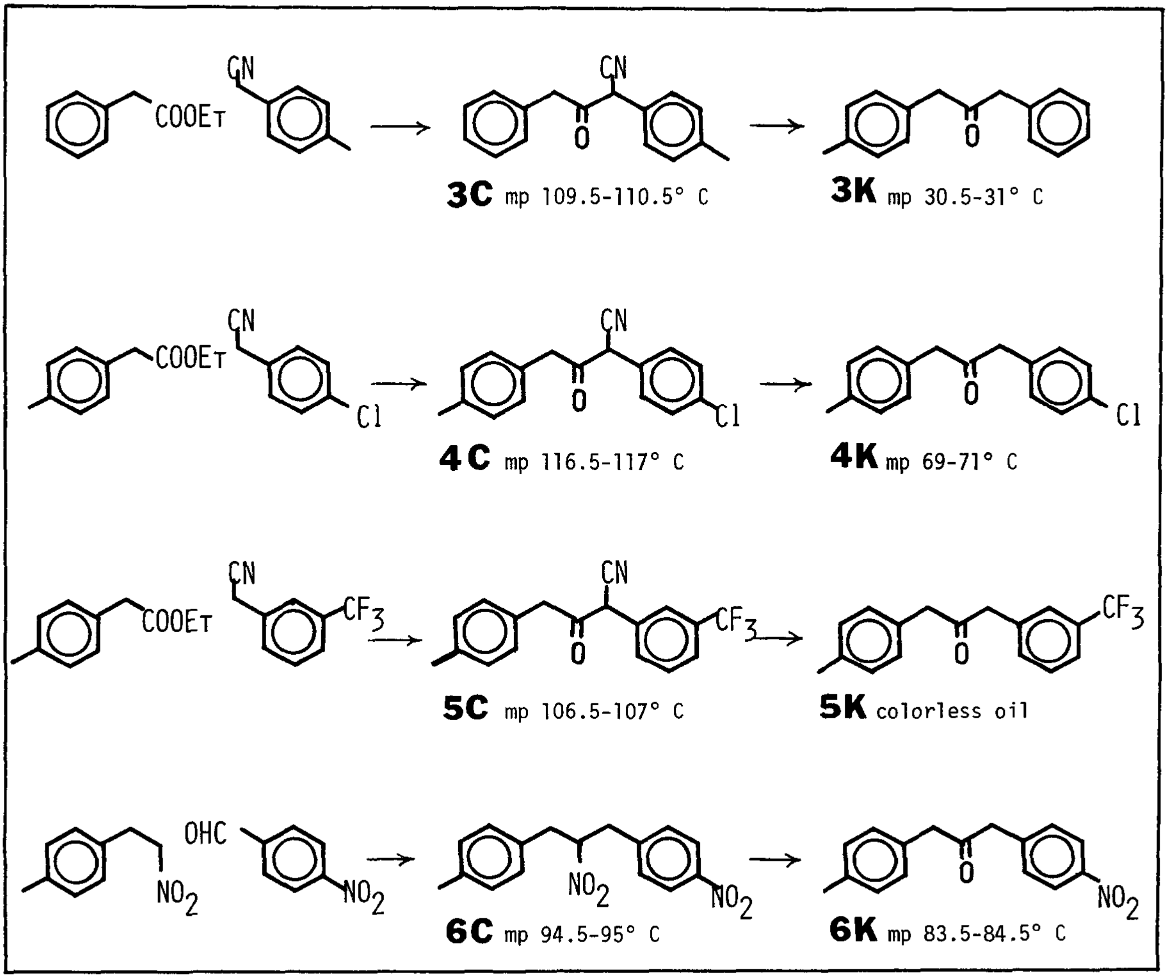
A

B

Compounds	Y	Z
3A , **3B**	CH_3	H
4A , **4B**	CH_3	p-Cl
5A , **5B**	CH_3	m-CF_3
6A , **6B**	CH_3	p-NO_2

Ketones 3K, 4K, and 5K were prepared by the Claisen condensation of a phenylacetic ester with a phenylacetonitrile (see Table I) followed by hydrolysis and decarboxylation of the β-keto nitrile.[6] Ketone 6K was made by the condensation of 2-p-tolylnitroethane with p-nitrobenzaldehyde followed by acetylation of the β-hydroxynitro compound; then $NaBH_4$ reduction (after in situ loss of HOAc) followed by $KMnO_4$ oxidation of the saturated nitro compound gave the ketone 6K.[7] Although it should be possible to prepare single chloro ketone isomers from intermediates 3C - 6C, for initial studies mixtures of the isomeric chloro ketones were used. These were made from each ketone by first generating the enol silyl ether (Et_3N, Me_3SiCl) and then treating it with a Cl_2/CCl_4 solution. For each pair the ^{1}H NMR signals for the methyl groups were separated, as were the CHCl ^{1}H NMR signals of three of the four pairs (3, 5, and 6 A,B). Peak assignments in the ^{1}H NMR spectra were made by comparing the spectra of all four mixtures and taking into account the known deshielding effect of chlorine and the substituents (see Table II).

Table I. Intermediates in the Synthesis of Chloro Ketones A and B.[7]



3C mp 109.5-110.5° C

3K mp 30.5-31° C

4C mp 116.5-117° C

4K mp 69-71° C

5C mp 106.5-107° C

5K colorless oil

6C mp 94.5-95° C

6K mp 83.5-84.5° C

The isomerization of each of the binary mixtures of monochloro ketones **3**-**6** **A**,**B** was examined at room temperature in $CDCl_3$ saturated with HCl gas in sealed NMR tubes. Progress was followed by integrating the CH_3 and CHCl proton signals. Equilibration was judged by no further change in composition after a suitable period and by insuring that raising the temperature to 80°C for many weeks did not change the ratio of chloro ketones noticeably.[8]

The equilibrium constants are listed in Table II. In spite of the saturated sp^3 character of the α- and α'-carbons, there is a considerable polar effect on the relative stability of the two chloro ketones which is greatest for the **Y** = Me, **Z** = NO_2 pair **6** **A**,**B** ($K_{B/A}$ = 4.9) corresponding to ΔG 0.95 kcal./mol. at room temperature (25°C). Since the only difference between the **A** and **B** isomers is the reversed location of a C-Cl and a C-H bond, the substituent effect must be transmitted (mostly through space) to these two bonds. The effect should be much greater on the bond to the more electronegative chlorine atom. For this reason we regard the substituent effect as being directed primarily to the C-Cl bond, which as would be expected prefers the α-position closer to the more electron-donating (Me) substituent.[9]

Table II. ^1H NMR Data and Equilibrium Constants for Chloro Ketones **3**-**6** **A**, **B**.

Compound	δ CH_3-Ar	δ H-CCl	Normalized Integration Area	$K_{eq.}$ (B/A)
3A	2.28	5.44	48	1.1
3B	2.33	5.42	52	
4A	2.30	5.38	36	1.9
4B	2.34	"	68	
5A	2.30	5.46	29	2.4
5B	2.35	5.44	71	
6A	2.32	5.50	17	4.9
6B	2.36	5.44	83	

It is gratifying that log K_{eq} correlates linearly (r = 0.998) with the <u>difference</u> in Taft $\sigma°$ values for the substituents with ρ = +0.75 (Fig. 1).[10] For the few substituents used so far, the correlation (r = 0.995) is also just as good with the difference in Hammett σ values except that the line does not pass through the origin. The correlation with σ_I and σ^* was poor.

The encouraging outcome of this work has thus provided the first reaction which can be used to study quantitatively electronic effects on carbon-chlorine bonds in an equilibrium situation.

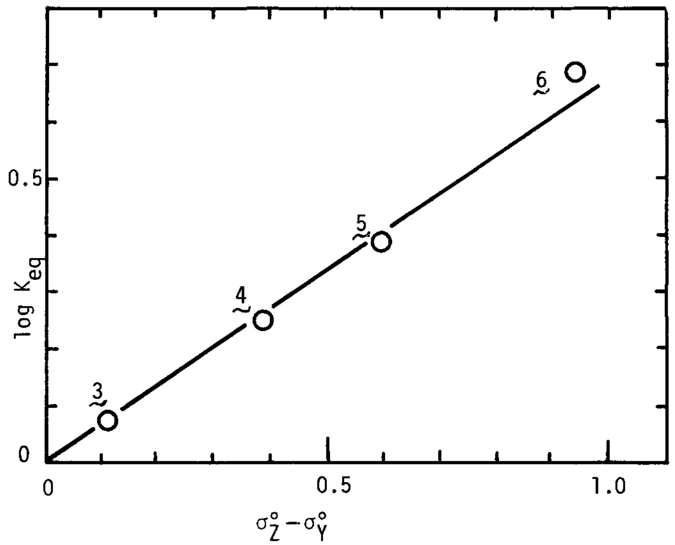


Figure 1. Hammett plot of log K_{eq} for A$\rightleftharpoons$B *vs*. $\sigma^\circ_Z-\sigma^\circ_Y$.
σ°: CH_3 -0.12, *p*-Cl 0.27, *m*-CF_3 0.47, *p*-NO_2 0.82.[10]

REFERENCES and NOTES

1. α-Halo Ketones XI. For part X see V. Dave and E.W. Warnhoff, J. Org. Chem., **48**, 2590 (1983).
2. E.W. Warnhoff, M. Rampersad, P. Sundara Raman, and F.W. Yerhoff, Tetrahedron Lett., 1659 (1978).
3. P. Metzger, A. Casadevall, and E. Casadevall, Tetrahedron, **31**, 469 (1975).
4. Although in some cases the reaction mixture can become highly colored, the colored material is present in negligible amount from ^{1}H NMR examination.
5. Several other pairs of chlorodibenzyl ketones were prepared, but these pairs were not as amenable to analysis by ^{1}H NMR spectroscopy.
6. S.B. Coan and E.I. Becker, Org. Synth., Coll. Vol. **IV**, 174 (1963).
7. Satisfactory IR and ^{1}H NMR spectra and precise mass determinations on molecular ions were obtained for all compounds in Table I.
8. The nature of the chemical change being examined (A$\rightleftharpoons$B) insures that $\Delta S = 0$, and since $T\Delta S = 0$, K_{eq} will not be temperature dependent.
9. This interpretation is couched in the terms commonly used by organic chemists. It would be equally possible to state the argument in terms of an effect on the total energy of the molecule caused by dipole-dipole interaction of substituents and chlorine atom, e.g. NO_2, CH_3 and Cl in **5A**,**B**.
10. O. Exner in Advances in Linear Free Energy Relationships, ed. by N.B. Chapman and J. Shorter, Plenum Press, London, 1972, p.32.

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